STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 123038

TO: Rei-Tsang Shiao **Location: 5a10 / 5c18** **Wednesday, May 26, 2004** **Art Unit: 1626** **Phone: 272-9797** **Serial Number: 10 / 629865**	**From: Jan Delaval** **Location: Biotech-Chem Library** **Rem 1A51** **Phone: 272-2504** **jan.delaval@uspto.gov**

Search Notes

Jan Velgar
effort search

123038

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Robert (Reg) Shiu Examiner #: 79524 Date: 5/26/04
Art Unit: 1626 Phone Number: 2-0707 Serial Number: 10/62 98165
Mail Box and Bldg Room Location: KM 5A10/5C18 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Process for producing (3R-5S)
Inventors (please provide full names): Yokuhama et al

Earliest Priority Filing Date:

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

1. Search a process for making of IV by

formula (I)
OR
formula (II)
OR
formula (III)

+ cell
microorganism
reducing

→ cpd IV

II formula (I) → (II') (III')

see claims 2-3

STAFF USE ONLY

Searcher: Jan
Searcher Phone #: 22504
Searcher Location:
Date Searcher Picked Up: 5/26
Date Completed: 5/26
Searcher Prep & Review Time:
Clerical Prep Time: 10
Online Time: 30

Type of Search

NA Sequence (#):
AA Sequence (#):
Structure (#): ✓
Bibliographic:
Litigation:
Fulltext:
Patent Family:
Other:

Vendors and cost where applicable

STN ✓
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

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=> fil reg
FILE 'REGISTRY' ENTERED AT 15:46:04 ON 26 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   25 MAY 2004  HIGHEST RN 685826-98-6
DICTIONARY FILE UPDATES:  25 MAY 2004  HIGHEST RN 685826-98-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d sta que l3
L1              STR
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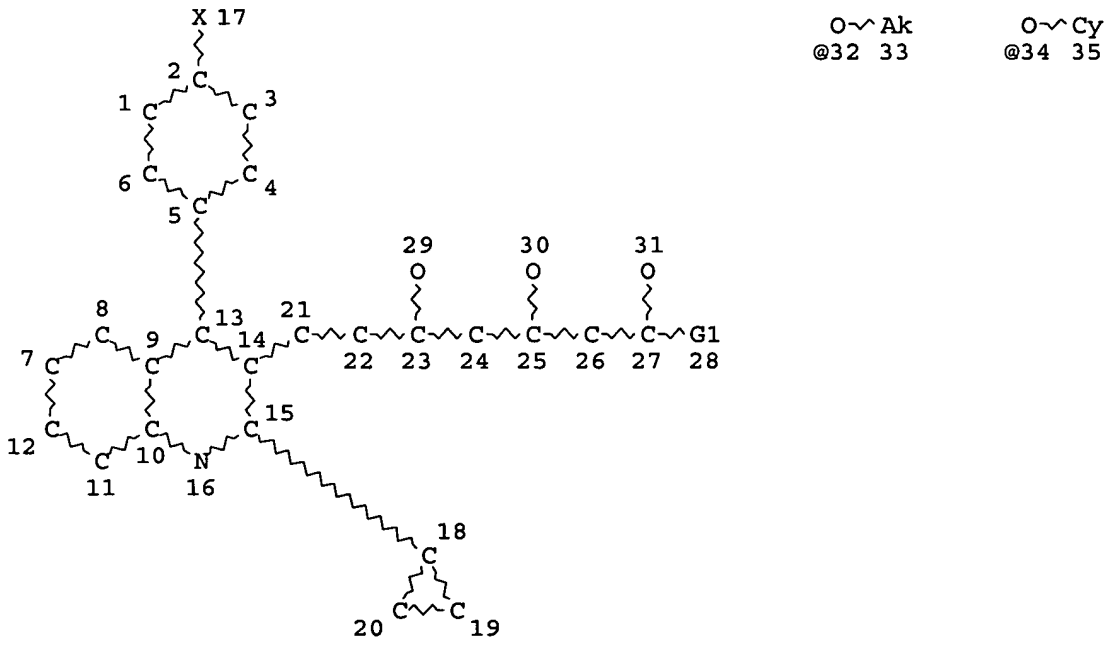


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VAR G1=OH/32/34
NODE ATTRIBUTES:
CONNECT IS M1  RC AT  35
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  35

STEREO ATTRIBUTES: NONE
L3           74 SEA FILE=REGISTRY CSS FUL L1
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100.0% PROCESSED    374 ITERATIONS                    74 ANSWERS
SEARCH TIME: 00.00.01


=> d his

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L2               3 S L1 CSS
L3              74 S L1 CSS FUL
               SAV L3 SHIAO629/A TEMP

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               E HARA M/AU
L7             412 S E3,E19
               E TAKUMA Y/AU
L8              91 S E3,E17,E21
               E KATSURADA M/AU
L9              39 S E3,E5
               E HOSOKAWA A/AU
L10             33 S E3,E4
               E MATSUMOTO Y/AU
L11            489 S E3
               E MATSUMOTO YOU/AU
L12             14 S E4
               E KASUGA Y/AU
L13             50 S E3,E33
               E WATANABE N/AU
L14            595 S E3,E4,E62
L15              1 S L5 AND L6
L16              2 S L5 AND L7-L14
L17              2 S L15,L16
L18             34 S L5 AND (MITSUBISHI? OR NISSAN?)/PA,CS
L19              2 S L17 AND L18
               SEL HIT RN

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L22             39 S L3(L)PREP+NT/RL
L23             39 S L3/P
L24             21 S L21 AND L22,L23
               E MICROORGANISM/CW
L25              1 S E3,E4,E5 AND L21
               E MICROORGANISM/CT
               E E3+ALL
L26              1 S E3,E4,E2+NT AND L21
L27              1 S L25,L26
L28              3 S L22,L23 AND ?MICROORG?
L29              3 S L27,L28
               E METSCHNIKOWIA/CT
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L30             1 S E3+OLD,NT,PFT AND L21
                  E CRYPTOCOCCUS/CT
                  E E3+ALL
L31             1 S L21 AND (E1+OLD,NT,PFT OR E2+OLD,NT,PFT OR E3+OLD,NT,PFT)
                  E CANDIDA/CT
L32             1 S E3+OLD,NT,PFT AND L21
                  E FILOBASIDIUM/CT
L33             1 S E3+OLD,NT,PFT AND L21
                  E OGATAEA/CT
L34             1 S E3+OLD,NT,PFT AND L21
                  E CITEROMYCES/CT
L35             1 S E3+OLD,NT,PFT AND L21
L36             1 S E4+OLD,NT,PFT AND L21
L37             0 S E5+OLD,NT,PFT AND L21
                  E YARROWIA/CT
L38             1 S E3+OLD,NT,PFT AND L21
L39             1 S E5+OLD,NT,PFT AND L21
                  E RHODOTORULA/CT
L40             1 S E3+OLD,NT,PFT AND L21
                  E EXOPHIALA/CT
L41             1 S E3+OLD,NT,PFT AND L21
                  E TRIGONOPSIS/CT
L42             1 S E3+OLD,NT,PFT AND L21
L43             1 S E4+OLD,NT,PFT AND L21
                  E SHIZOSACCHAROMYCES/CT
                  E SCHIZOSACCHAROMYCES/CT
L44             1 S E3+OLD,NT,PFT AND L21
                  E WICKERHAMIELLA/CT
L45             1 S E3+OLD,NT,PFT AND L21
                  E PICHIA/CT
L46             1 S E3+OLD,NT,PFT AND L21
                  E SACCHAROMYCOPSIS/CT
L47             1 S E3+OLD,NT,PFT AND L21
                  E SAITOELLA/CT
L48             1 S E3+OLD,NT,PFT AND L21
                  E SACCHAROMYCES/CT
L49             1 S E3+OLD,NT,PFT AND L21
                  E RHODOSPORIDIUM/CT
L50             1 S E3+OLD,NT,PFT AND L21
                  E ACINETOBACTER/CT
L51             1 S E3+OLD,NT,PFT AND L21
                  E BREVIBACTERIUM/CT
L52             1 S E3+OLD,NT,PFT AND L21
                  E CELLULOMONAS/CT
L53             1 S E3+OLD,NT,PFT AND L21
                  E CORYNEBACTERIUM/CT
L54             1 S E3+OLD,NT,PFT AND L21
                  E CURTOBACTERIUM/CT
L55             1 S E3+OLD,NT,PFT AND L21
L56             3 S L19,L25-L55
L57             3 S L56 AND L5-L19,L21-L56
L58             1 S L5 AND (BREVIBACTER? OR CELLULOMON? OR CORYNEBACTER? OR CURTO
L59            10 S L5 AND (METSCHNIKOW? OR CRYPTOCOC? OR CANDIDA? OR FILOBASID?
L60            10 S L19,L25-L59
L61             2 S L60 AND L21
L62             3 S L19,L61
L63             7 S L60 NOT L62
L64             1 S L63 AND MICROORGANISM
L65             4 S L62,L64

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     FILE 'HCAPLUS' ENTERED AT 15:45:19 ON 26 MAY 2004
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L66 3 S L65 NOT ITAVASTATIN

FILE 'REGISTRY' ENTERED AT 15:46:04 ON 26 MAY 2004

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 15:46:11 ON 26 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 26 May 2004 VOL 140 ISS 22
FILE LAST UPDATED: 25 May 2004 (20040525/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

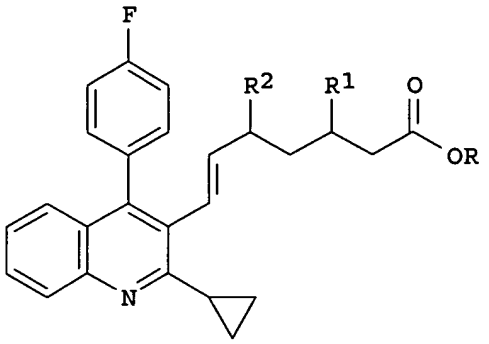
=> d all hitstr tot l66

L66 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:757860 HCAPLUS
DN 139:272910
ED Entered STN: 26 Sep 2003
TI Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcohols
IN Hiraoka, Hirotoshi; Ueda, Makoto; **Hara, Mari**
PA **Mitsubishi Chemical Corporation, Japan; Nissan Chemical Industries, Ltd.**
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C12N015-53
ICS C12N009-04; C12N001-21; C12P017-02; C12P041-00; C12R001-645; C12R001-19
CC 7-2 (Enzymes)
Section cross-reference(s): 3, 10, 16
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003078634	A1	20030925	WO 2003-JP3262	20030318

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2003339387 A2 20031202 JP 2003-74017 20030318
PRAI JP 2002-75921 A 20020319
GI



I

AB Provide a novel carbonyl reductase originating in a microorganism belonging to the genus Ogataea, an encoding gene, recombinant expression, and use for producing optically active alcs. By reducing ketones having general structures I (R = H, alkyl, aryl; R1 = :O, OH, (R)-OH; R2 = OH, (S)-OH, :O) with the use of carbonyl reductase, optically active alcs., in particular, (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid esters, can be produced. A novel carbonyl reductase was isolated from Ogataea minuta var. nonfermentans strain IFO 1473. Its substrate specificity was investigated with various ketones and aldehydes. Its activity for reduction of 2,2,2-Trifluoroacetophenone was significantly inhibited by Hg(I) ion and Zn(II) ion. Its gene was cloned, sequenced, and expressed in E. coli. The recombinant enzyme was used in production of. (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid Et ester (3R,5S-DOLE) from (E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dioxo-hept-6-enoic acid Et ester (DOXE) or 5S-(E)-7-[2-cyclopropyl-4-(fluorophenyl)-quinolin-3-yl]-5-hydroxy-3-oxohepto-6-enoic acid Et ester (5S-MOLE), is described. The yield was 319 μg (31.9% with 100% e.e. optical purity), and 807 μg (80.7% with 97% e.e. optical purity), resp.

ST carbonyl reductase gene Ogataea optically active alc

IT Asymmetric synthesis and induction
DNA sequences
Molecular cloning
Ogataea minuta nonfermentans
Protein sequences
(Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)

IT Alcohols, preparation
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)

IT Gene, microbial
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)

IT Reduction
(enzymic, stereoselective; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)

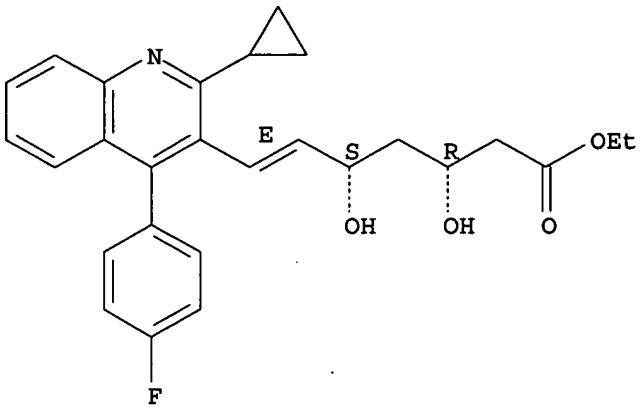
IT Purity
(optical; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)

IT Escherichia coli
(recombinant expression in; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
IT Aldehydes, biological studies
Ketones, biological studies
RL: BCP (Biochemical process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(reduction of; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
IT **167073-19-0P**, (3R,5S)-(E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid ethyl ester
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
IT 77106-95-7P, Carbonyl reductase
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); CAT (Catalyst use); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
IT 22542-11-6, biological studies 23713-49-7, Zinc ion, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reduction of 2,2,2-Trifluoroacetophenone inhibited by; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
IT **166803-31-2**, (E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dioxo-hept-6-enoic acid ethyl ester **254452-91-0**, 5S-(E)-7-[2-Cyclopropyl-4-(fluorophenyl)-quinolin-3-yl]-5-hydroxy-3-oxohepto-6-enoic acid ethyl ester
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(reduction of, substrate; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
IT 89-98-5, o-Chlorobenzaldehyde 93-55-0, Propiophenone 94-02-0, Ethylbenzoyl acetate 99-02-5, m-Chloroacetophenone 99-61-6, m-Nitrobenzaldehyde 99-91-2, p-Chloroacetophenone 104-88-1, p-Chlorobenzaldehyde, biological studies 431-03-8, Diacetyl 434-45-7, 2,2,2-Trifluoroacetophenone 532-27-4, 2-Chloroacetophenone 552-89-6, o-Nitrobenzaldehyde 587-04-2, m-Chlorobenzaldehyde 600-14-6, 2,3-Pentanedione 645-59-0, Benzylacetonitrile 822-87-7, 2-Chlorocyclohexanone 1694-29-7, 3-Chloro-2,4-pentadione 2142-63-4, m-Bromoacetophenone 5469-26-1, 1-Bromo-3,3-dimethyl-2-butanone 10409-46-8, 2-Chloro-2-Methylcyclohexanone 13031-04-4 20201-24-5, Ethyl-3-methyl-2-oxobutanoate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(reduction of, substrate; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
IT 606130-03-4 606130-04-5 606130-05-6 606130-06-7
RL: PRP (Properties)
(unclaimed sequence; ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Mitsubishi Chemical Corp; WO 02063028 A1 2002 HCAPLUS
(2) Mitsubishi Chemical Corp; JP 2002300897 A 2002 HCAPLUS
(3) Nissan Chemical Industries Ltd; JP 01-279866 A 1989 HCAPLUS
(4) Nissan Chemical Industries Ltd; EP 304063 A2 1989 HCAPLUS
(5) Nissan Chemical Industries Ltd; US 5011930 A 1989 HCAPLUS
(6) Nissan Chemical Industries Ltd; JP 08-127585 A 1996 HCAPLUS
(7) Nissan Chemical Industries Ltd; JP 08-92217 A 1996 HCAPLUS
IT **167073-19-0P**, (3R,5S)-(E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxy-hept-6-enoic acid ethyl ester
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP

(Preparation)
(Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)

RN 167073-19-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

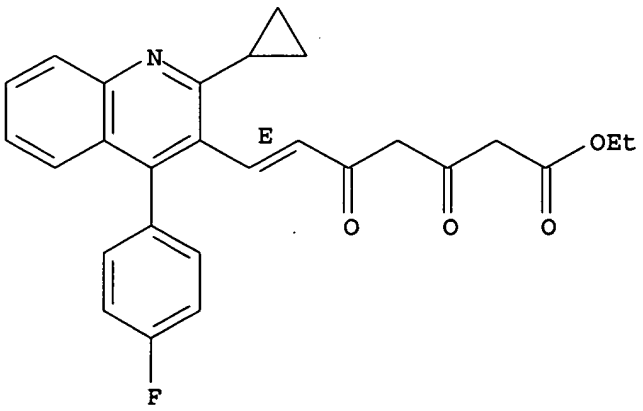
Absolute stereochemistry.
Double bond geometry as shown.



IT **166803-31-2**, (E)-7-[2-Cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dioxo-hept-6-enoic acid ethyl ester **254452-91-0**, 5S-(E)-7-[2-Cyclopropyl-4-(fluorophenyl)-quinolin-3-yl]-5-hydroxy-3-oxohepto-6-enoic acid ethyl ester
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(reduction of, substrate; Ogataea minuta carbonyl reductase, encoding gene, and use for producing optically active alcs.)

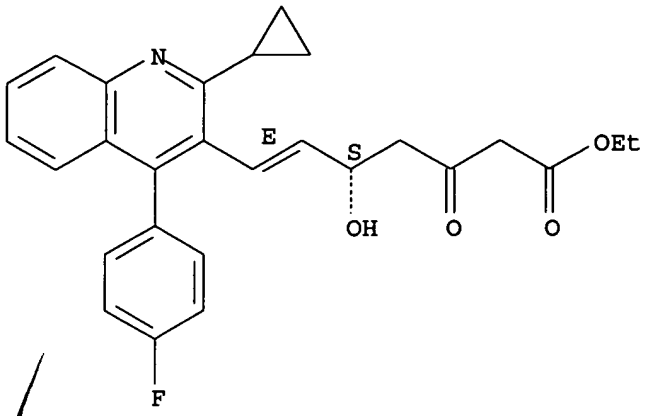
RN 166803-31-2 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 254452-91-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L66 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:663303 HCAPLUS
DN 139:178816
ED Entered STN: 26 Aug 2003
TI Optically active hydroxyketo esters manufacture with **microorganism**
IN Asano, Yasuhisa; Suzuki, Kenji; Matsumoto, Hiroo
PA **Nissan Chemical Industries, Ltd., Japan**
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C12P017-12
ICS C12R001-84; C12R001-645; C12R001-865
CC 16-2 (Fermentation and Bioindustrial Chemistry)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2003235595	A2	20030826	JP 2002-38670	20020215
PRAI JP 2002-38670		20020215		

OS MARPAT 139:178816
AB The title optically active hydroxyketo esters (I) are manufactured by asym. reduction with **microorganism** such as **Saccharomyces** cerevisiae. I, especially (3R,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3-hydroxy-5-oxy-6-heptanoic acid Et ester, are useful intermediates for manufacture of HMG-CoA reductase inhibitors which are useful for preparing hypocholesteremics.
ST hydroxyketo ester manuf **Saccharomyces microorganism** hypocholesteremic intermediate
IT Resolution (separation)
(enzymic; optically active hydroxyketo esters manufacture with **microorganism** by asym. reduction)
IT Anticholesteremic agents
(intermediates for; optically active hydroxyketo esters manufacture with **microorganism** by asym. reduction)
IT Fermentation
Hansenula **wickerhamii**
Kuraishia
Ogataea
Pichia
Pichia angusta
Pichia anomala
Pichia capsulata
Pichia farinosa

Pichia naganishii
Saccharomyces
Saccharomyces cerevisiae
Yamadazyma
(optically active hydroxyketo esters manufacture with **microorganism** by asym. reduction)

IT Reduction
(stereoselective; optically active hydroxyketo esters manufacture with **microorganism** by asym. reduction)

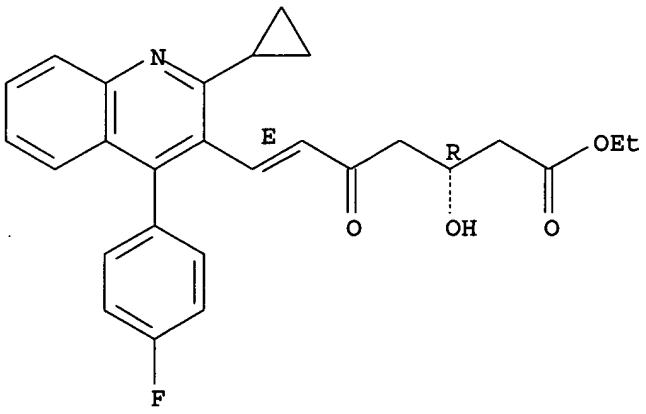
IT **444732-68-7P**
RL: **BPN (Biosynthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**
(optically active hydroxyketo esters manufacture with **microorganism** by asym. reduction)

IT **166803-31-2**
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(optically active hydroxyketo esters manufacture with **microorganism** by asym. reduction)

IT **444732-68-7P**
RL: **BPN (Biosynthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**
(optically active hydroxyketo esters manufacture with **microorganism** by asym. reduction)

RN 444732-68-7 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, ethyl ester, (3R,6E)- (9CI) (CA INDEX NAME)

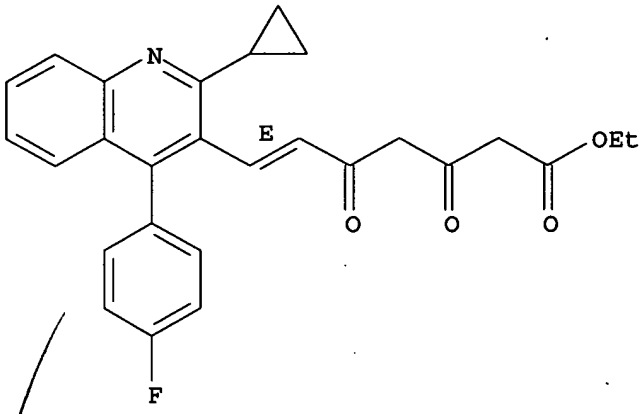
Absolute stereochemistry.
Double bond geometry as shown.



IT **166803-31-2**
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(optically active hydroxyketo esters manufacture with **microorganism** by asym. reduction)

RN 166803-31-2 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

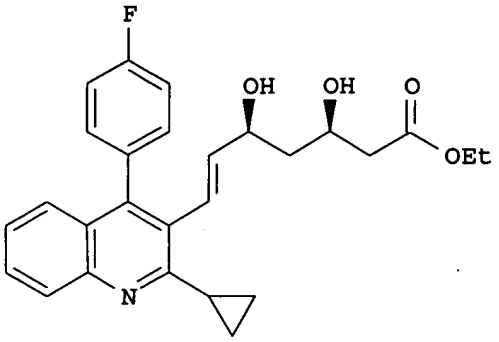


L66 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:615881 HCAPLUS
DN 137:139496
ED Entered STN: 16 Aug 2002
TI Process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivatives
IN **Hara, Mari; Takuma, Yuki; Katsurada, Manabu; Hosokawa, Akemi; Matsumoto, Youichi; Kasuga, Yuzo; Watanabe, Naoyuki**
PA **Mitsubishi Chemical Corporation, Japan; Nissan Chemical Industries, Ltd.**
SO PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C12P017-12
ICS C12P017-12; C12R001-645
CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002063028	A1	20020815	WO 2002-JP835	20020201 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	JP 2003137870	A2	20030514	JP 2001-331480	20011029 <--
	JP 2002300897	A2	20021015	JP 2002-25423	20020201 <--
	EP 1365029	A1	20031126	EP 2002-710461	20020201 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2004030139	A1	20040212	US 2003-629865	20030730 <--
PRAI	JP 2001-26316	A	20010202 <--		
	JP 2001-331480	A	20011029 <--		
	WO 2002-JP835	W	20020201 <--		

OS CASREACT 137:139496; MARPAT 137:139496
GI



I

AB A process for producing the title compound (I) and optically active derivs. with **microorganism** by fermentation was given. I is useful as serum cholesterol-reducing agent. Preparation of Et ester of I (3R,5S-DOLE) and its derivs. 3S,5R-, 3S,5S-, and 3R,5R-DOLE with **Saccharomycopsis** fibuligera from 5-Mol, i.e. 5-(E)-7-[2-cyclopropyl-4-(fluorophenyl)-quinolin-3-yl]-5-hydroxy-3-oxohepto-6-enoic acid Et ester was shown.

ST DOLE serum cholesterol reducing agent fermn **microorganism**; deriv DOLE fermn **microorganism Saccharomycopsis**

IT Reduction
(biochem., stereoselective; process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

IT Reduction
(enzymic, stereoselective; process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

IT Resolution (separation)
(enzymic; process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

IT **Acinetobacter**
Acinetobacter calcoaceticus
Anticholesteremic agents
Brevibacterium
Brevibacterium saccharolyticum
Candida
Candida albicans
Candida cylindracea
Candida famata
Candida famata famata
Candida intermedia
Candida molischiana
Candida parapsilosis
Candida solani
Candida tropicalis
Cellulomonas
Cellulomonas flavigena
Cellulomonas gelida
Cellulomonas uda
Citeromyces
Citeromyces matritensis
Corynebacterium
Corynebacterium acetoacidophilum
Corynebacterium ammoniagenes
Corynebacterium glutamicum
Corynebacterium vitaeruminis
Cryptococcus (fungus)

Cryptococcus curvatus
Cryptococcus flavus
Cryptococcus humicolus
Cryptococcus laurentii
Curtobacterium
Curtobacterium flaccumfaciens
Drugs
Exophiala
Exophiala dermatitidis
Fermentation
Filobasidium
Filobasidium capsuligenum
Metschnikowia
Metschnikowia bicuspidata
Metschnikowia pulcherrima
Metschnikowia reukaufii
Microorganism
Ogataea
Ogataea minuta
Ogataea minuta nonfermentans
Pichia
Pichia anomala
Pichia glucozyma
Pichia petersonii
Rhodosporidium
Rhodosporidium toruloides
Rhodotorula
Rhodotorula aurantiaca
Rhodotorula mucilaginosa
Saccharomyces
Saccharomyces cerevisiae
Saccharomycopsis
Saccharomycopsis fibuligera
Saitoella
Saitoella complicata
Schizosaccharomyces
Schizosaccharomyces pombe
Trigonopsis
Trigonopsis variabilis
Wickerhamiella
Wickerhamiella domercquii
Yarrowia
Yarrowia lipolytica
(process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

IT **148901-69-3 166803-31-2 444732-67-6 444732-68-7**
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

IT **147511-69-1P 167073-18-9P 167073-19-0P 380848-30-6P 380848-32-8P**
RL: **BPN (Biosynthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**
(process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

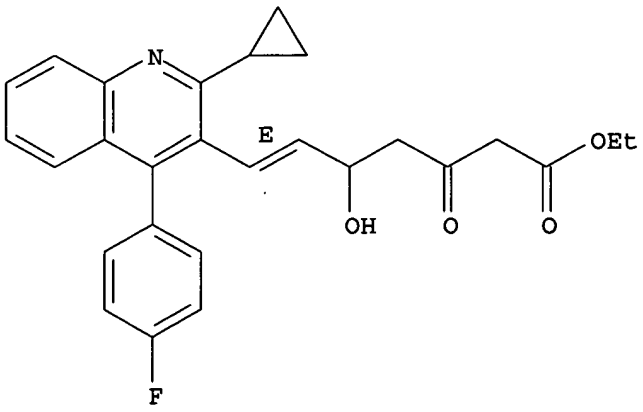
RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) E R Squibb & Sons Inc; CA 2094191 A 1993 HCAPLUS
(2) E R Squibb & Sons Inc; US 5324662 A 1993 HCAPLUS
(3) E R Squibb & Sons Inc; EP 569998 A2 1993 HCAPLUS
(4) E R Squibb & Sons Inc; JP 630783 A 1993

(5) Nagamatsu, S; J Chromatogr A 1999, V832, P55 HCAPLUS
(6) Nissan Chemical Industries Ltd; JP 01279866 A 1989 HCAPLUS
(7) Nissan Chemical Industries Ltd; EP 304063 A2 1989 HCAPLUS
(8) Nissan Chemical Industries Ltd; US 5011930 A 1989 HCAPLUS
(9) Nissan Chemical Industries Ltd; US 5102888 A 1989 HCAPLUS
(10) Nissan Chemical Industries Ltd; US 5185328 A 1989 HCAPLUS
(11) Nissan Chemical Industries Ltd; US 5854259 A 1989 HCAPLUS
(12) Nissan Chemical Industries Ltd; US 5856336 A 1989 HCAPLUS
(13) Nissan Chemical Industries Ltd; US 5872130 A 1989 HCAPLUS
(14) Ube Industries Ltd; JP 08127585 A 1996 HCAPLUS
(15) Ube Industries Ltd; JP 892217 A 1996

IT **148901-69-3 166803-31-2 444732-67-6**
444732-68-7
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)

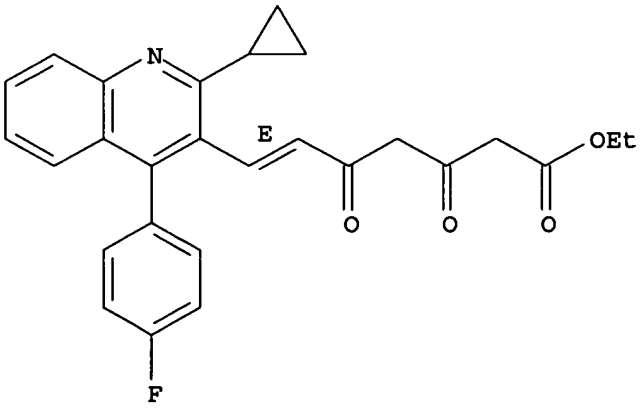
RN 148901-69-3 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



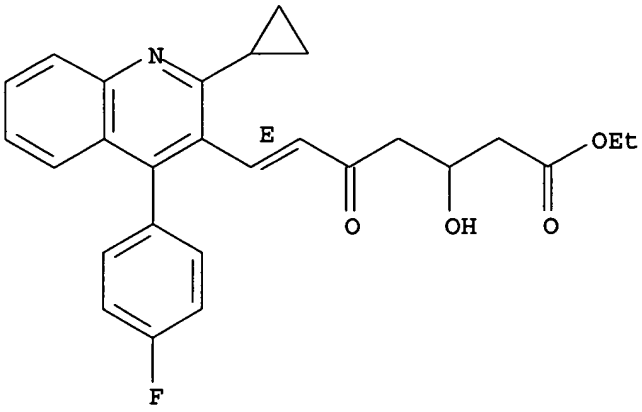
RN 166803-31-2 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



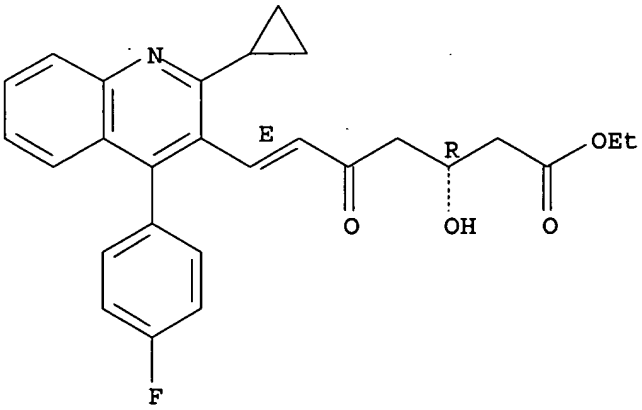
RN 444732-67-6 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



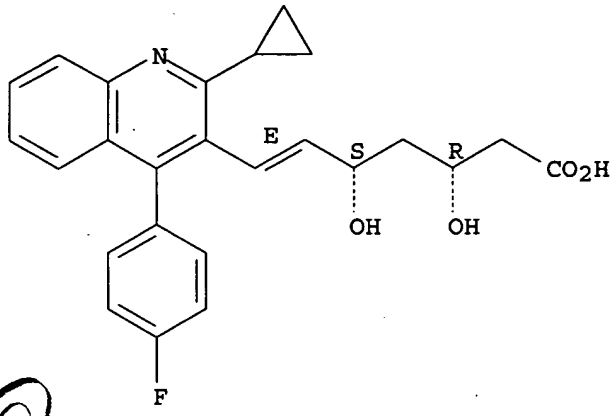
RN 444732-68-7 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, ethyl ester, (3R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



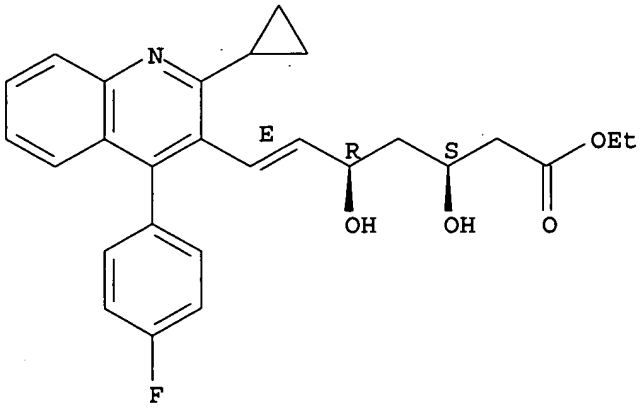
IT **147511-69-1P 167073-18-9P 167073-19-0P**
380848-30-6P 380848-32-8P
RL: **BPN (Biosynthetic preparation)**; BIOL (Biological study);
PREP (Preparation)
(process for producing (3R,5S)-(E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-quinolin-3-yl]-3,5-dihydroxyhept-6-enoic acid ester and derivs.)
RN 147511-69-1 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



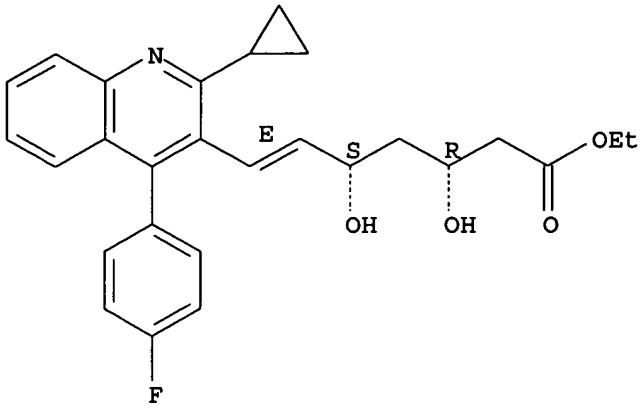
RN 167073-18-9 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



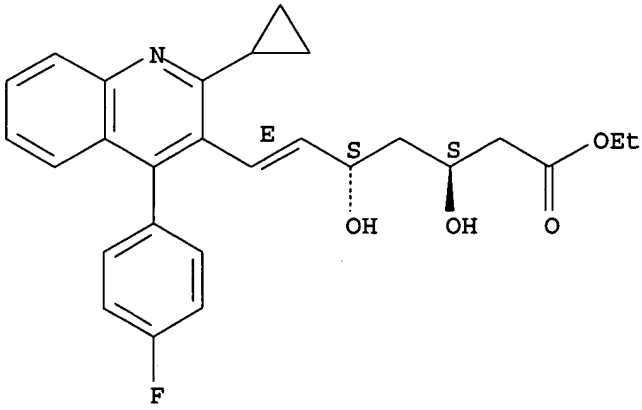
RN 167073-19-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



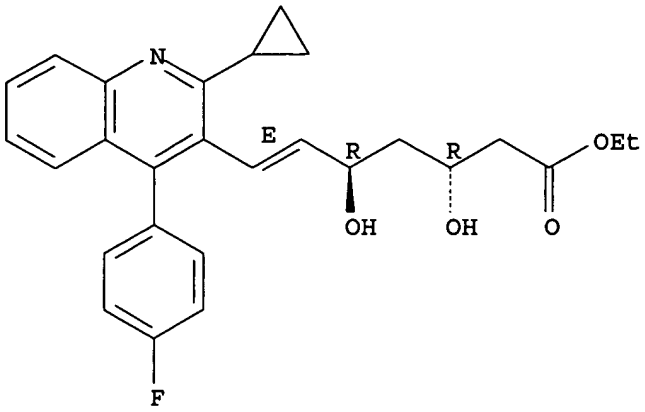
RN 380848-30-6 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 380848-32-8 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

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L67  ANSWER 1 OF 20  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:154436  HCAPLUS
DN   138:204870
TI   Processes for preparing calcium salt forms of statins
IN   Niddam-Hildesheim, Valerie; Lifshitz-Liron, Revital; Lidor-Hadas, Rami
PA   Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA,
     Inc.
SO   PCT Int. Appl., 32 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 4
     PATENT NO.          KIND  DATE           APPLICATION NO.  DATE
     ----------------    ----  --------       ---------------  --------
PI   WO 2003016317       A1    20030227       WO 2002-US26012  20020816
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
     US 2002099224       A1    20020725       US 2001-37412    20011024 <--
     US 6528661          B2    20030304
     US 2003114685       A1    20030619       US 2002-222556   20020816
PRAI US 2001-312812P     P     20010816
     US 2001-37412       A     20011024
     US 2000-249319P     P     20001116  <--
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     US 2001-326529P     P     20011001
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OS MARPAT 138:204870
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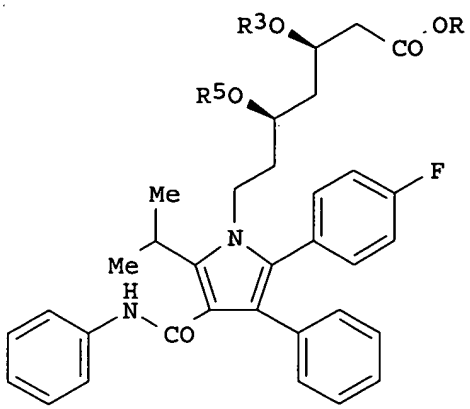


I

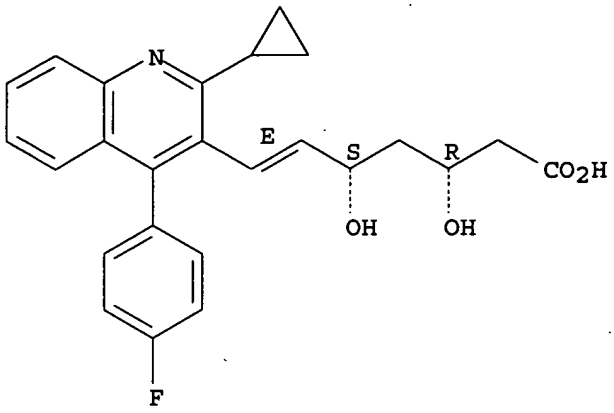
AB Processes for preparing hemicalcium salts of a statins RCH(OH)CH2CH(OH)CH2CO2H (R = statin organic radical selected from pravastatin, fluvastatin, cerivastatin, atorvastatin, rosuvastatin, pitavastatin, simvastatin, or lovastatin) from an ester derivative or protected ester derivative of the statin by using calcium hydroxide are provided. The ester or protected ester derivative is contacted with calcium hydroxide to obtain the calcium salt. Preferred statins are rosuvastatin, pitavastatin and atorvastatin, simvastatin and lovastatin. In processes beginning with a protected satin ester derivative, the protecting group is hydrolyzed during salt formation by contact with calcium hydroxide, or is contacted with an acid catalyst followed by contact with calcium hydroxide. Thus, diol-protected atorvastatin ester I (R = CMe3, R3R5 = CMe2) was treated with an 80% aqueous soln of AcOH at rt for 20 h to form the deprotected ester I (R = CMe3, R3 = R5 = H) which was in turn dissolved in EtOH, treated with a saturated soln of Ca(OH)2 containing Bu4N+Br- and stirred at 45° for 24 h to give atorvastatin hemicalcium salt I (R = 1/2Ca, R3 = R5 = H) in 77% yield for the two steps.

IT **147526-32-7P**, Pitavastatin hemicalcium
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(processes for preparing calcium salt forms of statins)

RN 147526-32-7 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

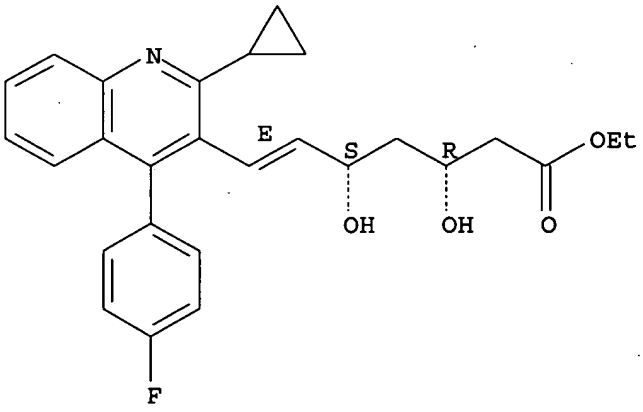
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



●1/2 Ca

IT **167073-19-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(processes for preparing calcium salt forms of statins)
RN 167073-19-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:293628 HCAPLUS
DN 136:325435
TI Process for producing optically active ethyl (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate
IN Onishi, Atsushi; Murazumi, Koichi; Tachibana, Kozo
PA Daicel Chemical Industries, Ltd., Japan; Nissan Chemical Industries, Ltd.
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002030903	A1	20020418	WO 2001-JP9000	20011012 <--
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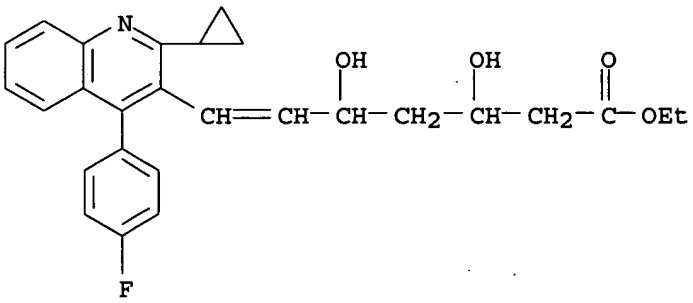
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001095926	A5	20020422	AU 2001-95926	20011012 <--
	EP 1334967	A1	20030813	EP 2001-976679	20011012 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	JP 2000-314245	A	20001013 <--		
	WO 2001-JP9000	W	20011012		

AB The process for producing an optically active isomer of Et 7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate comprises optically resolving, at a high efficiency, a mixture of optical isomers of the compound, characterized in that a packing comprising a support and cellulose tris(4-chlorophenylcarbamate) deposited thereon in a specific proportion is used to chromatog. isolate the target isomer under such conditions as to result in a specific retention volume The title compound is an intermediate for the known hypolipemic NK 104.

IT **121661-13-0**
RL: ANT (Analyte); ANST (Analytical study)
(process for producing optically active Et (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate)

RN 121661-13-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)

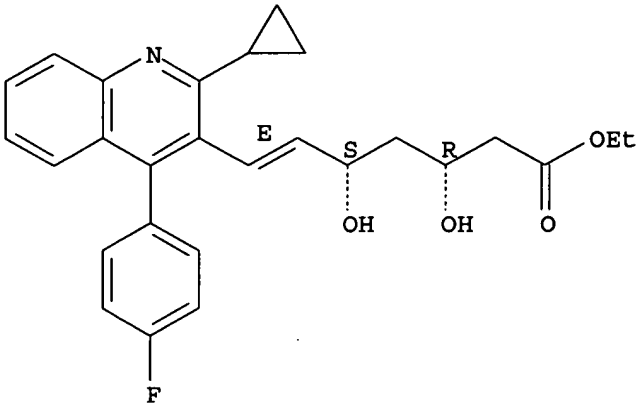


IT **167073-19-0P**
RL: ANT (Analyte); **PUR (Purification or recovery)**; ANST (Analytical study); **PREP (Preparation)**
(process for producing optically active Et (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate)

RN 167073-19-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

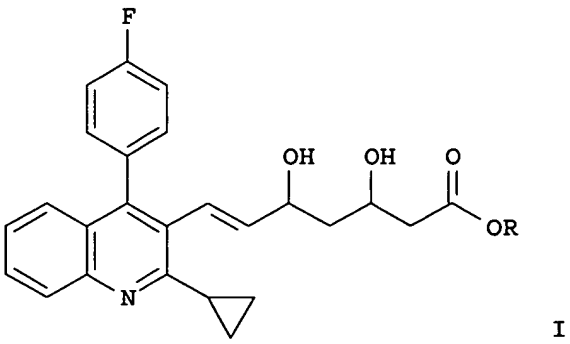


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:932409 HCAPLUS
DN 136:36497
TI Manufacture of (3R,5S,6E)-7-(substituted-quinolyl)-3,5-dihydroxyhept-6-enoic acid esters by stereoselective enzymic hydrolysis
IN Tokuda, Shinichiro; Okabe, Toshiyuki; Soma, Tamotsu
PA Nissan Chemical Industries, Ltd., Japan; Sankyo Kasei Kogyo K. K.
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	JP 2001352996	A2	20011225		JP 2000-175316	20000612	<--
PRAI	JP 2000-175316		20000612	<--			

OS MARPAT 136:36497
GI



I

AB The compds. (3R,5S,6E)-I (R = C1-4 alkyl) (II), useful as intermediates for (3R,5S,6E)-7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolyl]-3,5-dihydroxyhept-6-enoic acid salts as hypolipemics and antiatherosclerotics, are manufactured by treating a mixture of stereoisomers of (6E)-I including II with acylating agents in the presence of hydrolases, removing the hydrolases from the reaction mixture, and then separating II from the mixture

A

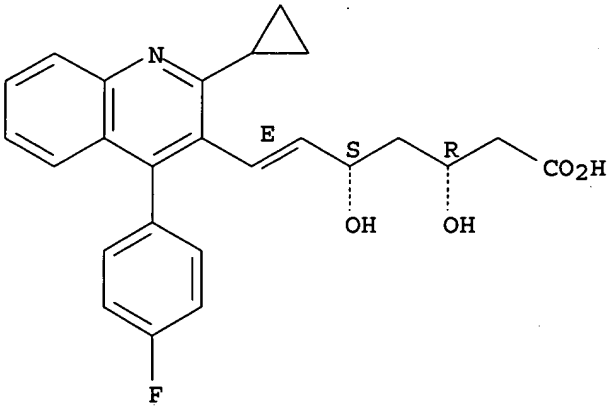
mixture (3.37 g) of II (R = Et) 49.7, (3S,5R,6E)-I (R = Et) 49.7, (3S,5S,6E)-I (R = Et) <0.3, and (3R,5R,6E)-I (R = Et) <0.3% was treated with isopropenyl acetate and Lipase PS in Me3COMe at 40° for 94 h to give 1,40 g II (R = Et) with 99.4% e.e.

IT **147511-69-1DP**, salts
RL: **PNU (Preparation, unclassified); PREP (Preparation)**
(hypolipemics, intermediates for; manufacture of optically-active quinolyldihydroxyheptenoic acid esters from stereoisomer mixts. using acylating agents and hydrolases)

RN 147511-69-1 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

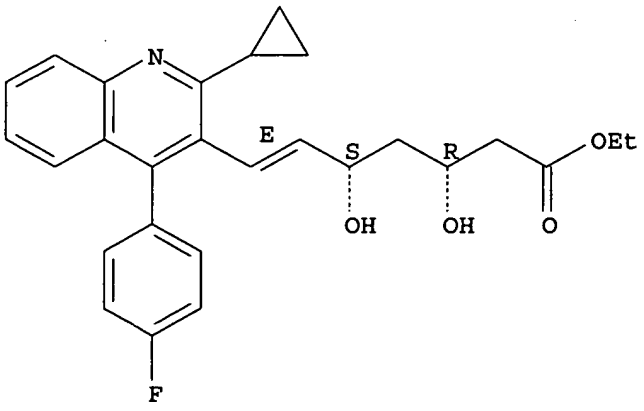


IT **167073-19-0P**
RL: **PUR (Purification or recovery); PREP (Preparation)**
(manufacture of optically-active quinolyldihydroxyheptenoic acid esters from stereoisomer mixts. using acylating agents and hydrolases)

RN 167073-19-0 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

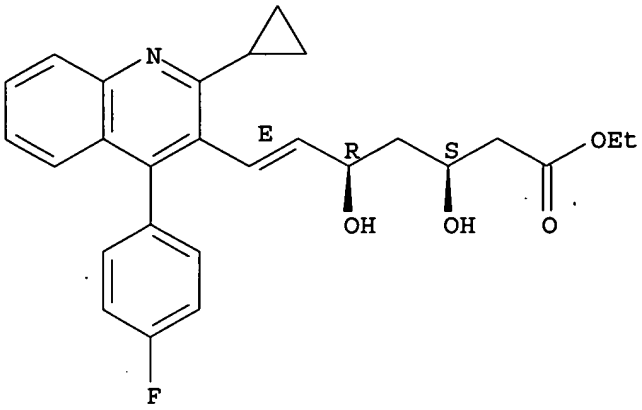


IT **167073-18-9 380848-30-6 380848-32-8**
RL: RCT (Reactant); RACT (Reactant or reagent)

(manufacture of optically-active quinolyldihydroxyheptenoic acid esters from stereoisomer mixts. using acylating agents and hydrolases)

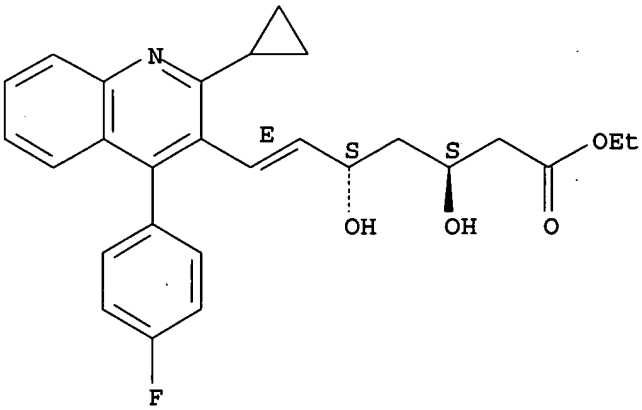
RN 167073-18-9 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



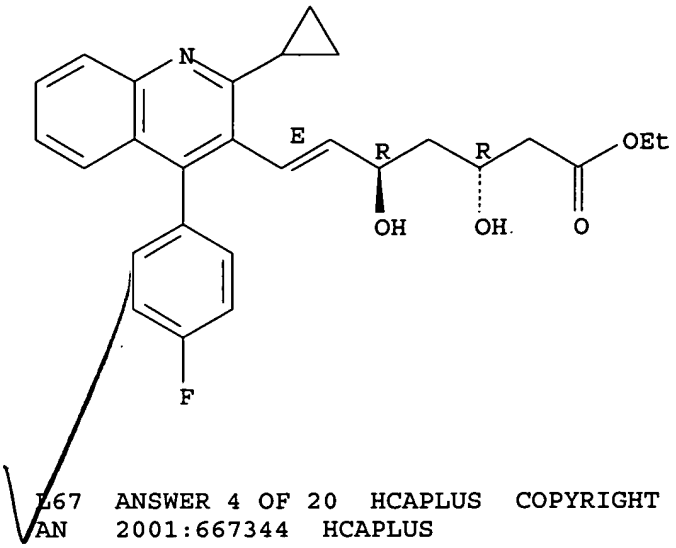
RN 380848-30-6 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



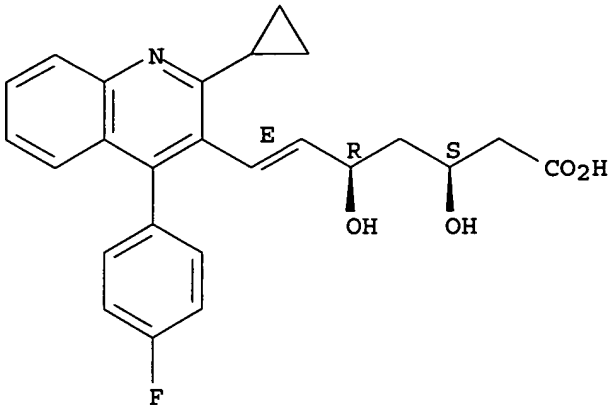
RN 380848-32-8 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L67 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:667344 HCAPLUS
DN 136:112193
TI Synthesis and biological evaluations of quinoline-based HMG-CoA reductase inhibitors
AU Suzuki, M.; Iwasaki, H.; Fujikawa, Y.; Kitahara, M.; Sakashita, M.; Sakoda, R.
CS Central Research Laboratories, Nissan Chemical Industries, Ltd., Funabashi, Chiba, 274-8507, Japan
SO Bioorganic & Medicinal Chemistry (**2001**), 9(10), 2727-2743
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
AB A series of quinoline-based 3,5-dihydroxyheptenoic acid derivs. were synthesized from quinolinecarboxylic acid esters by homologation, aldol condensation with Et acetoacetate dianion, and reduction of 3-hydroxyketone to evaluate their ability to inhibit the enzyme HMG-CoA reductase in vitro. In agreement with previous literature, a strict structural requirement exists on the external ring, and 4-fluorophenyl is the most active in this system. For the central ring, substitution on positions 6, 7, and 8 of the central quinoline nucleus moderately affected the potency, whereas the alkyl side chain on the 2-position had a more pronounced influence on activity. Among the derivs., NK-104 (pitavastatin calcium), which has a cyclopropyl group as the alkyl side chain, showed the greatest potency. We found that further modulation and improvement in potency at inhibiting HMG-CoA reductase was obtained by having the optimal substituents flanking the desmethylmevalonic acid portion, i.e., 4-fluorophenyl and cyclopropyl, instead of the usual iso-Pr group.
IT **391681-56-4P**
RL: PAC (Pharmacological activity); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)** ; USES (Uses)
(synthesis and biol. evaluations of quinoline-based HMG-CoA reductase inhibitors)
RN 391681-56-4 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, monosodium salt, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

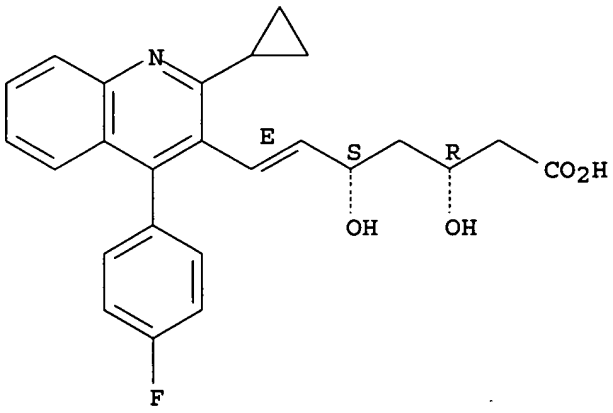
Relative stereochemistry.
Double bond geometry as shown.



● Na

IT **147526-32-7**, NK-104
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis and biol. evaluations of quinoline-based HMG-CoA reductase inhibitors)
RN 147526-32-7 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

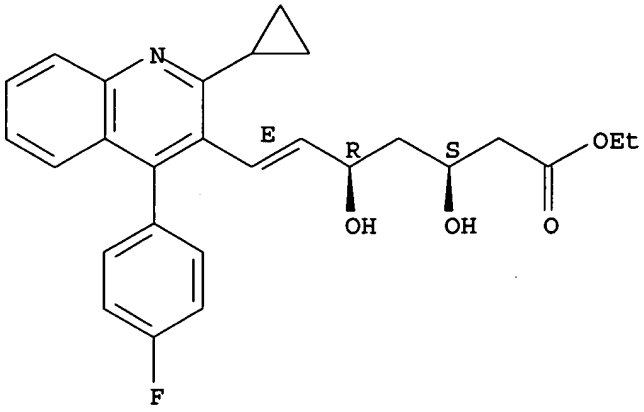
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



●1/2 Ca

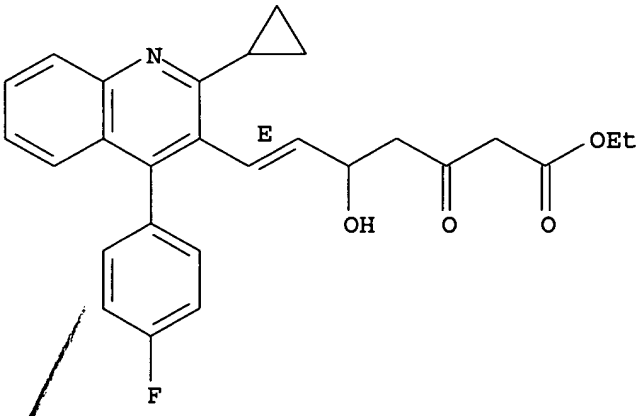
IT **147008-20-6P 148901-69-3P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(synthesis and biol. evaluations of quinoline-based HMG-CoA reductase inhibitors)
RN 147008-20-6 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 148901-69-3 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:84775 HCAPLUS
DN 132:122527
TI Process for the preparation of quinoline derivative and intermediate therefor
IN Ohara, Yoshio; Suzuki, Mikio; Yanagawa, Yoshinobu; Takada, Yasutaka
PA Nissan Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000005213	A1	20000203	WO 1999-JP3923	19990722 <--

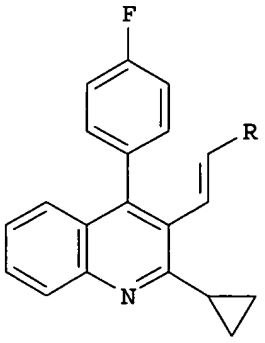
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU,

ID, IL, IN, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO,
NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

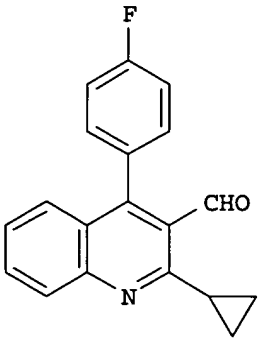
	CA 2338334	AA	20000203	CA 1999-2338334	19990722	<--
	AU 9947992	A1	20000214	AU 1999-47992	19990722	<--
	AU 746722	B2	20020502			
	EP 1099694	A1	20010516	EP 1999-931484	19990722	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	NZ 509401	A	20020828	NZ 1999-509401	19990722	<--
	CN 1107670	B	20030507	CN 1999-809003	19990722	<--
	RU 2214402	C2	20031020	RU 2001-105200	19990722	<--
	ZA 2001000525	A	20010801	ZA 2001-525	20010118	<--
	NO 2001000357	A	20010122	NO 2001-357	20010122	<--
	US 6335449	B1	20020101	US 2001-764994	20010123	<--
PRAI	JP 1998-207911	A	19980723	<--		
	WO 1999-JP3923	W	19990722	<--		

OS CASREACT 132:122527

GI



I



II

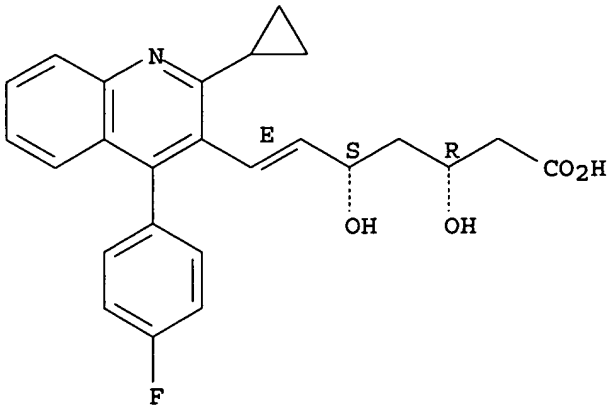
AB Claimed is a process for the preparation of 3-quinolinylpropenal derivative (I; R = CHO) through quinolylacrylonitrile I (R = cyano) which can be prepared by reacting quinolinealdehyde (II) with di-Et cyanomethyl phosphonate. I (R = CHO) is useful as an intermediate for a cholesterol-lowering agent (HMG-CoA reductase inhibitor) (III.1/2Ca). Thus, 400 g 20% aqueous NaOH was added dropwise to a mixture of II 199, di-Et cyanomethylphosphonate 136, and Aliquat 336 5.5 g in 960 g PhMe at 25-35° over 0.5-1 h and stirred at the same temperature for 1 h to give, after workup and recrystn. from hexane, 88% I (R = cyano). The latter nitrile (181 g) was dissolved in 1,812 mL PhMe and cooled to -10°, followed by adding a 1.02 M solution of diisobutylaluminum (664 mmol, 650 mL) at -10° to -5° over 1 h, and the resulting mixture was stirred at the same temperature for 1 h to give, after workup and recrystn. from a mixture of cyclohexane and n-hexane, 93% I (R = CHO).

IT **147526-32-7P**

RL: **PNU (Preparation, unclassified)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of quinolinylpropenal derivative by condensation of quinolinealdehyde derivative with di-Et cyanomethylphosphonate and reduction of

quinolylacrylonitrile derivative)
RN 147526-32-7 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



●1/2 Ca

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

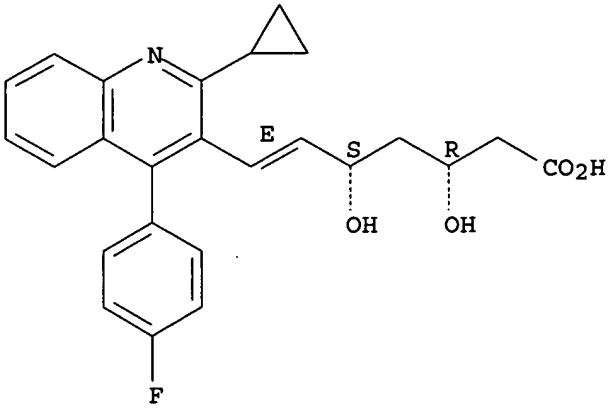
L67 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:716678 HCAPLUS
DN 132:93197
TI First systematic chiral syntheses of two pairs of enantiomers with 3,5-dihydroxyheptenoic acid chain, associated with a potent synthetic statin NK-104
AU Suzuki, Mikio; Yanagawa, Yoshinobu; Iwasaki, Hiroshi; Kanda, Hiroyasu; Yanagihara, Kazufumi; Matsumoto, Hiroo; Ohara, Yoshio; Yazaki, Yukari; Sakoda, Ryozo
CS Central Research Institute, Nissan Chemical Industries Ltd., Chiba, 274-8507, Japan
SO Bioorganic & Medicinal Chemistry Letters (**1999**), 9(20), 2977-2982
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 132:93197
AB All 4 enantiomers of the synthetic statin NK-104 were prepared The syn diol isomers (NK-104 and its enantiomer) were obtained efficiently by diastereomer resolution The anti diol isomers (3-epimer and 5-epimer) were prepared effectively by asym. aldol reaction followed by anti stereoselective reduction as key steps. Their purity detns. were effected by chiral HPLC anal.
IT **147511-70-4P 254452-87-4P 254452-91-0P 254452-95-4P**
RL: **PUR (Purification or recovery)**; RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of the enantiomers of NK-104)
RN 147511-70-4 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)-, compd. with (αR)-α-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 147511-69-1
CMF C25 H24 F N O4

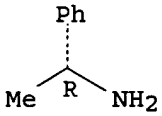
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

CRN 3886-69-9
CMF C8 H11 N

Absolute stereochemistry.

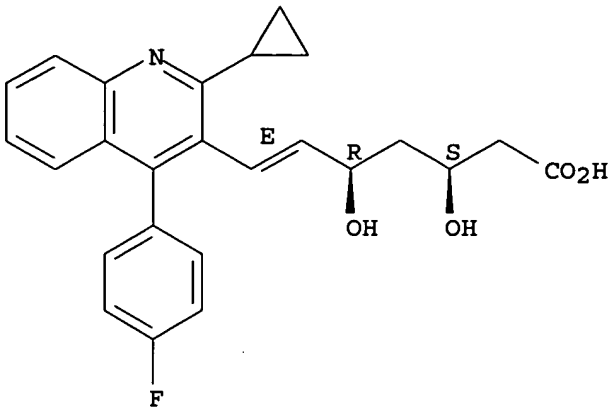


RN 254452-87-4 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3S,5R,6E)-, compd. with (αS)-α-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 254452-86-3
CMF C25 H24 F N O4

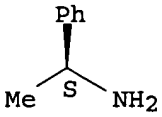
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



CM 2

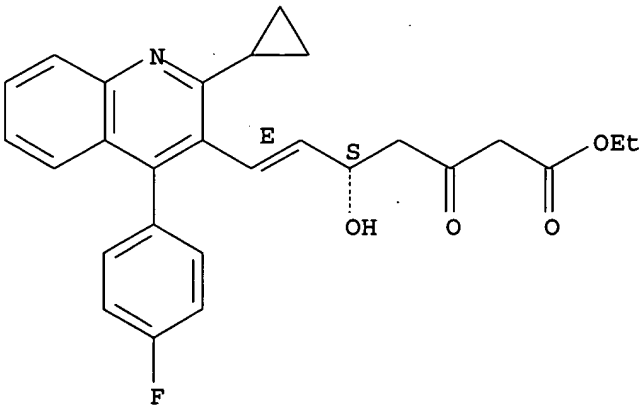
CRN 2627-86-3
CMF C8 H11 N

Absolute stereochemistry.



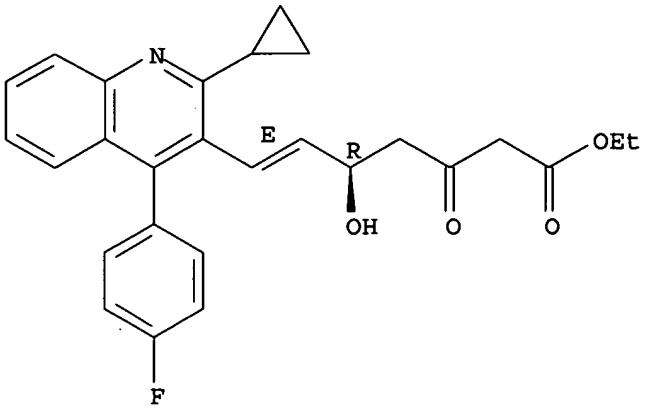
RN 254452-91-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 254452-95-4 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

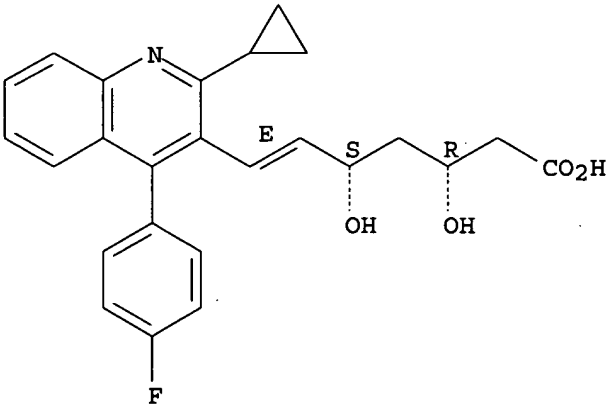


IT **147526-32-7P**, NK-104 **254452-88-5P**, ent-NK-104
254452-92-1P, 3-epi-NK-104 **254452-96-5P**, 5-epi-NK-104
RL: **PUR (Purification or recovery)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of the enantiomers of NK-104)

RN 147526-32-7 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

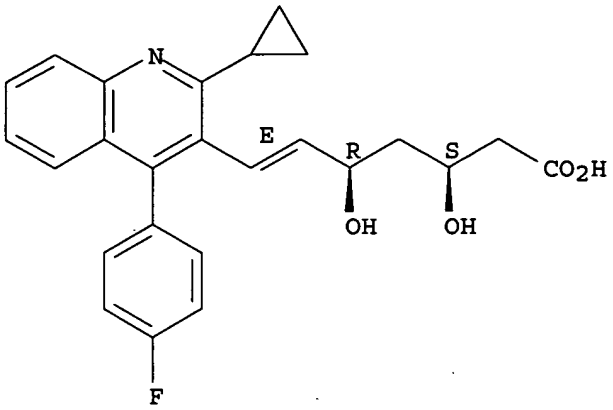


●1/2 Ca

RN 254452-88-5 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3S,5R,6E)- (9CI) (CA INDEX NAME)

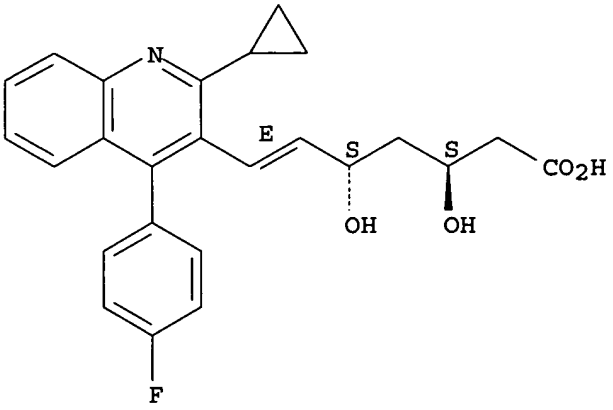
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



●1/2 Ca

RN 254452-92-1 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3S,5S,6E)- (9CI) (CA INDEX NAME)

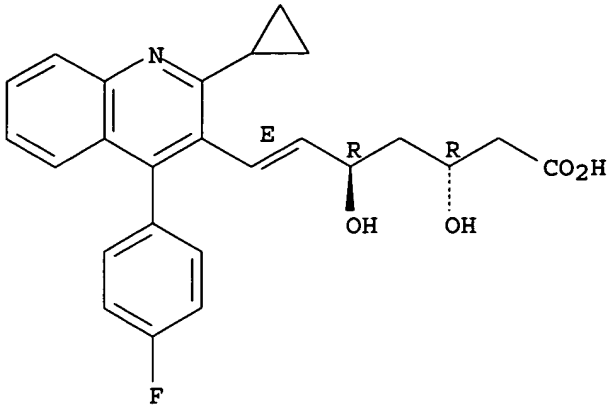
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



●1/2 Ca

RN 254452-96-5 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5R,6E)- (9CI) (CA INDEX NAME)

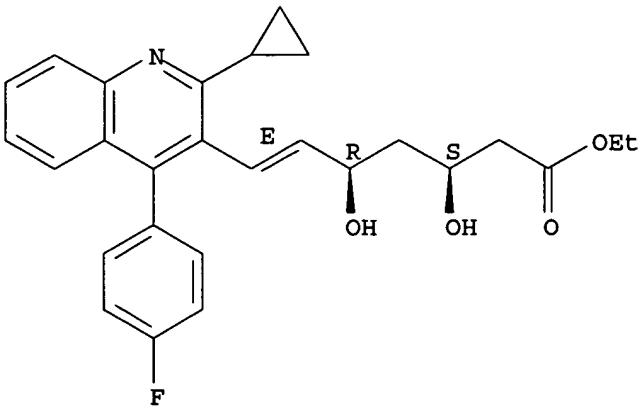
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



●1/2 Ca

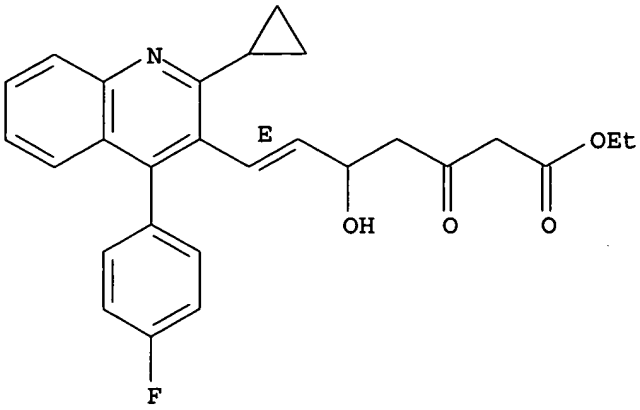
IT **147008-20-6P 148901-69-3P**
RL: RCT (Reactant); **SPN (Synthetic preparation); PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of the enantiomers of NK-104)
RN 147008-20-6 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



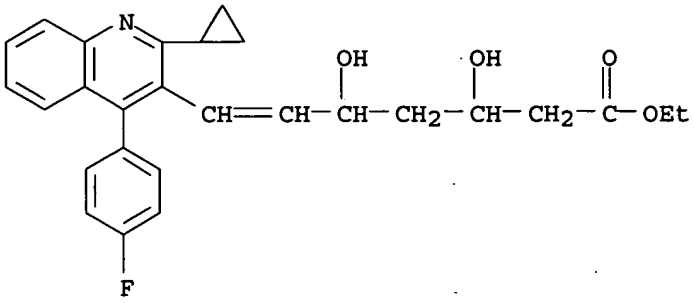
RN 148901-69-3 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

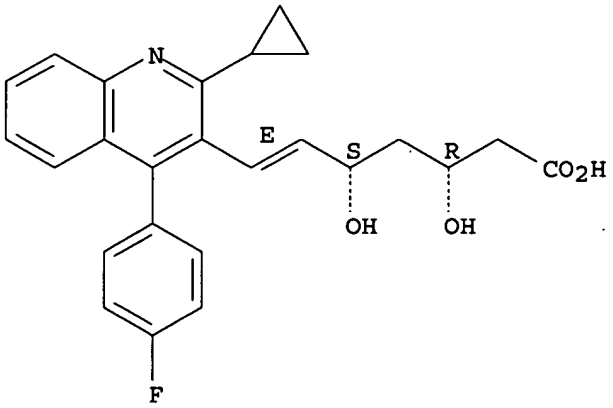
L67 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:96840 HCAPLUS
DN 130:316585
TI Chiral separation of a pharmaceutical intermediate by a simulated moving bed process
AU Nagamatsu, S.; Murazumi, K.; Makino, S.
CS Daicel Chemical Ind., Chiyoda-ku, Tokyo, 100, Japan
SO Journal of Chromatography, A (**1999**), 832(1 + 2), 55-65
CODEN: JCRAEY; ISSN: 0021-9673
PB Elsevier Science B.V.
DT Journal
LA English
AB The chiral separation of a pharmaceutical intermediate by a simulated moving bed (SMB) system on a pilot-scale is described. The operating conditions were chosen from results simulated by the software, help, developed by Novasep, based upon data from a single column. The productivity of the SMB system is tested by the separation of an ester of quinoline mevalonic acid at various internal flow-rates. The eluent consumption is also discussed. The step time to switch the ports to enter or withdraw solns. is one of important factors influencing the productivity.
IT **121661-13-0P**, DOLE
RL: ANT (Analyte); **PUR (Purification or recovery)**; THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(chiral separation of pharmaceutical intermediate by simulated moving bed process)
RN 121661-13-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L67 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:767327 HCAPLUS
DN 130:60508
TI NK-104: hypolipidemic HMG-CoA reductase inhibitor
AU Sorbera, L. A.; Leeson, P. A.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (**1998**), 23(8), 847-859
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review, with 42 refs., of the synthesis, pharmacol., pharmacokinetics, and clin. studies of the title agents.
IT **147526-32-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MSC (Miscellaneous); **PNU (Preparation, unclassified)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(hypolipidemic HMG-CoA reductase inhibitor)
RN 147526-32-7 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



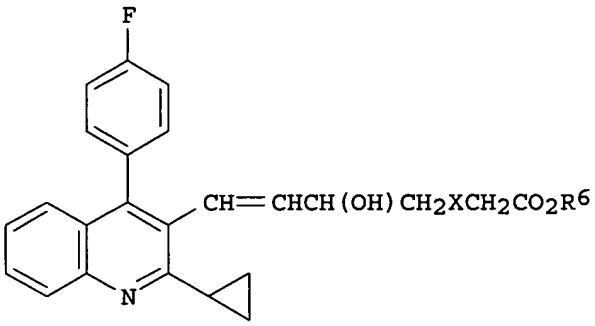
●1/2 Ca

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

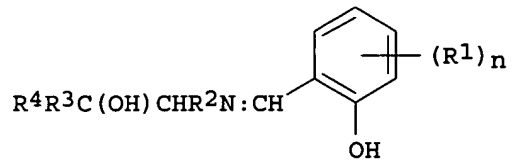
L67 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:409680 HCAPLUS
DN 125:58345
TI Preparation of optically active quinolyldihydroxyheptenoates as intermediates for anticholesteremics
IN Harada, Katsumasa; Matsushita, Akio; Sasaki, Hiroshi; Kawachi, Yasuhiro
PA Ube Industries, Japan; Nissan Chemical Ind Ltd
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 08092217	A2	19960409	JP 1994-212958	19940906 <--
PRAI JP 1994-212958		19940906 <--		

OS CASREACT 125:58345; MARPAT 125:58345
GI



I



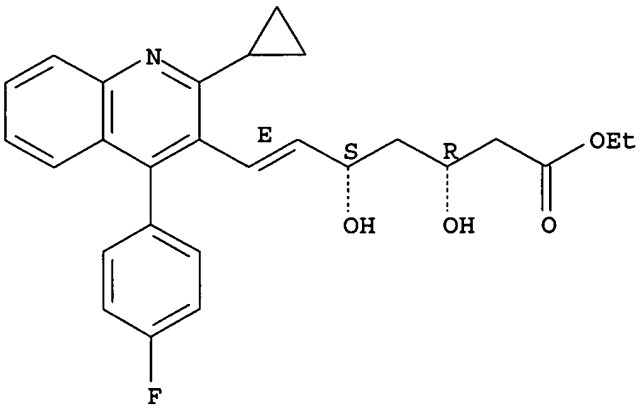
II

AB The title compds. I (R6 = alkyl, Ph; X = CHOH) are prepared by reaction of (E)-3-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]prop-2-en-1-al (III) with diketene in organic solvents in the presence of Ti complexes, prepared from optically active Schiff bases II (R1 = alkyl; R2 = H, alkyl, Ph; R3, R4 = H, alkyl; R2 = R3 = R4 ≠ H; n = 0-4) and Ti(OR5)4 (R5 = alkyl, Ph), followed by syn-reduction of the optically active I (X = CO). III and diketene were added to a mixture of (S)-II (R1 = 3-CMe3, R2 = CHMe2, R3-4 = H) and Ti(OEt)4 in CH2Cl2 and stirred at -50° for 62 h to give 72% (5S)-(E)-I (R6 = Et, X = CO) with 78% ee, reduction of which with NaBH4 and Me2BOMe in THF-MeOH at -75° for 3.5 h gave 88% (3R,5S)-(E)-I (R6 = Et, X = CHOH) (IV). IV was converted into (4R,6S)-(E)-6-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-ylethenyl]-4-hydroxy-3,4,5,6-tetrahydro-2H-pyran-2-one in 89% yield and 78% ee.

IT **167073-19-0P**
RL: **IMF (Industrial manufacture)**; RCT (Reactant); **SPN**

(Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of optically active quinolyldihydroxyheptenoates from quinolylpropenal and diketene by addition with Ti complexes and reduction)
RN 167073-19-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

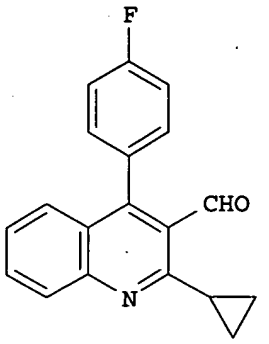
Absolute stereochemistry.
Double bond geometry as shown.



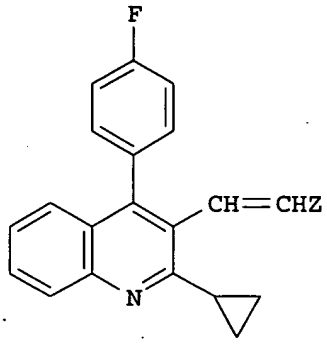
L67 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:281632 HCAPLUS
DN 124:343135
TI Preparation of quinolinaldehyde derivative as intermediate for quinoline type mevalonolactones
IN Matsumoto, Hiroo; Kanda, Hiroyasu; Obara, Yoshio; Ikeda, Hirokazu; Murakami, Tatsufumi
PA Daiseru Kagaku Kogyo Kk, Japan; Nitsusan Kagaku Kogyo Kk
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 08003138	A2	19960109	JP 1995-35587	19950223 <--
PRAI JP 1994-28596		19940225 <--		

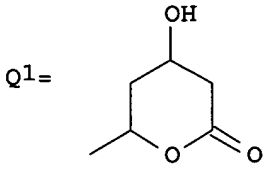
OS MARPAT 124:343135
GI



I



II

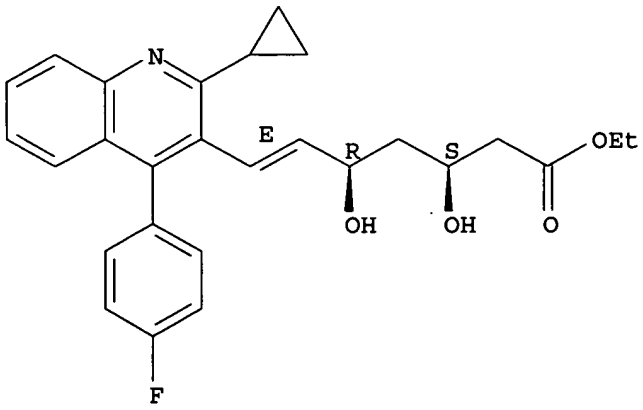


AB The title compound I is prepared by reaction of olefin II [Z = Q1, etc.] with ozone. Thus, a mixture of ozone and oxygen was introduced into II [Z = Q1] in ethanol and methanol at -60 to -72° during 1.5 h. Dimethylsulfide was then added to the reaction mixture at -72°; and the resulting mixture was warmed to room temperature during 1 h to give, after workup, 29% I.

IT **167073-18-9P 167073-19-0P**
RL: **PUR (Purification or recovery); PREP (Preparation)**
(preparation of quinolinaldehyde derivative as intermediate for quinoline type
mevalonolactones)

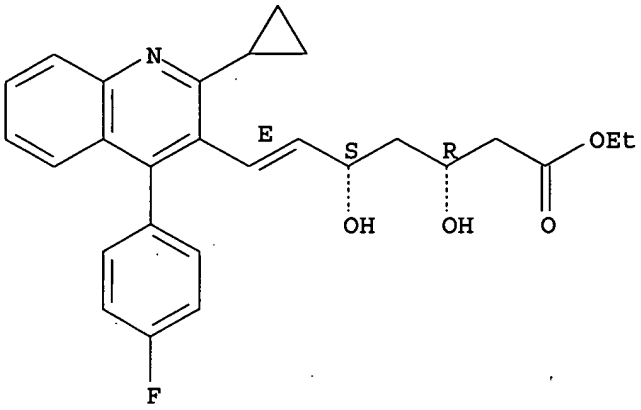
RN 167073-18-9 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

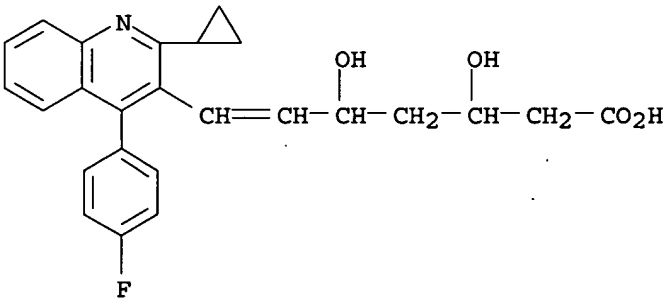


RN 167073-19-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

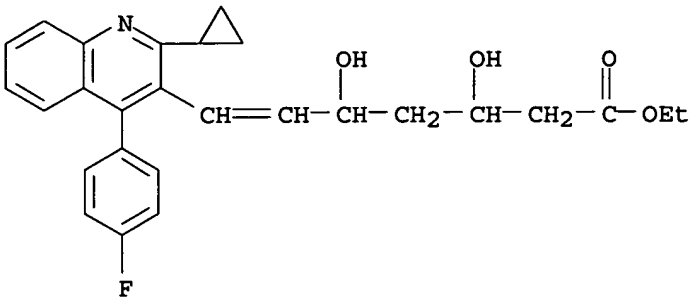


IT **121659-04-9 121661-13-0 148885-99-8**
148901-69-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinolinaldehyde derivative as intermediate for quinoline type
mevalonolactones)
RN 121659-04-9 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, monosodium salt (9CI) (CA INDEX NAME)

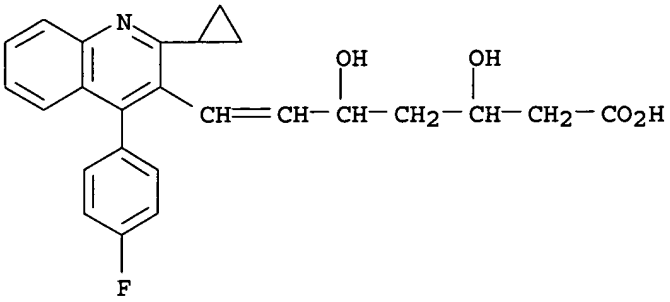


● Na

RN 121661-13-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



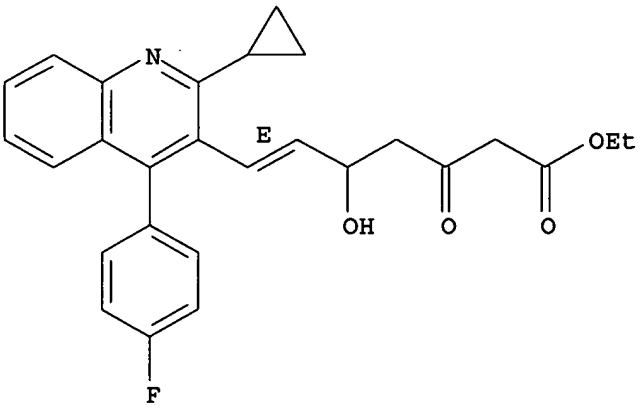
RN 148885-99-8 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1) (9CI) (CA INDEX NAME)



●1/2 Ca

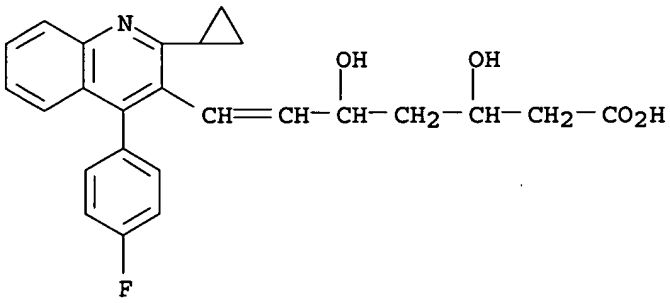
RN 148901-69-3 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT **121659-03-8P 176593-07-0P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of quinolinaldehyde derivative as intermediate for quinoline type

mevalonolactones)
RN 121659-03-8 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)

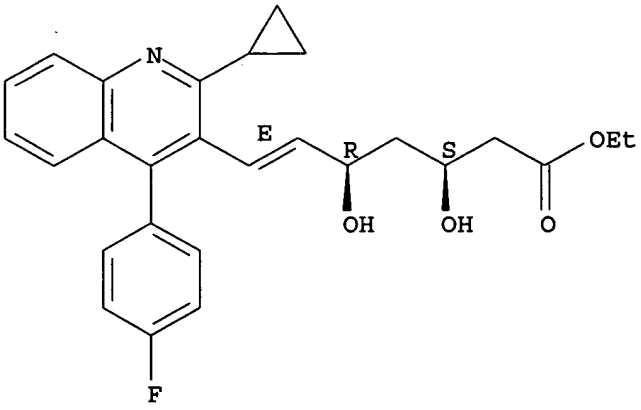


RN 176593-07-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, [R-[R*,S*-(E)]]-, compd. with (R)-α-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 167073-18-9
CMF C27 H28 F N O4

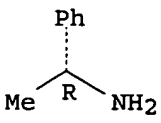
Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 3886-69-9
CMF C8 H11 N

Absolute stereochemistry.



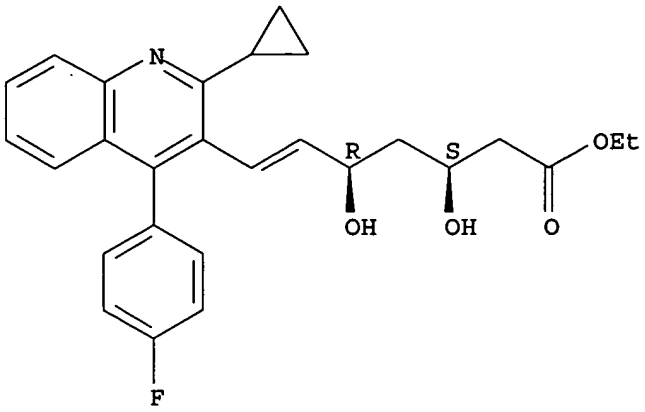
L67 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:994304 HCAPLUS
DN 124:86587
TI Process for producing optically active aromatic mevalonolactone compounds
IN Ikeda, Hirokazu; Murakami, Tatsushi; Matsumoto, Hiroo; Ohara, Yoshio; Kanda, Hiroyashu
PA Daicel Chemical Industries, Ltd., Japan; Nissan Chemical Industries, Ltd.
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9523125	A1	19950831	WO 1995-JP251	19950222 <--
	W: AU, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, RO, RU, SI, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2183071	AA	19950831	CA 1995-2183071	19950222 <--
	CA 2183071	C	20011218		
	AU 9518231	A1	19950911	AU 1995-18231	19950222 <--
	AU 691582	B2	19980521		
	EP 747341	A1	19961211	EP 1995-909953	19950222 <--
	EP 747341	B1	20020522		
	R: AT, CH, DE, FR, GB, IT, LI, NL				
	HU 74486	A2	19970128	HU 1996-2291	19950222 <--
	HU 214160	B	19980128		
	AT 217859	E	20020615	AT 1995-909953	19950222 <--
	CN 1136182	B	20040128	CN 1995-191678	19950222 <--
	US 5939552	A	19990817	US 1996-700396	19960822 <--
PRAI	JP 1994-28594	A	19940225 <--		
	WO 1995-JP251	W	19950222 <--		

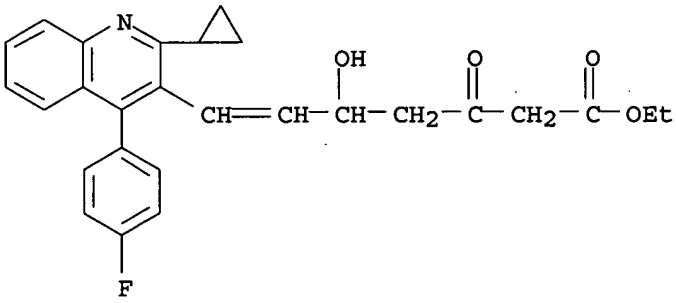
AB A mevalonolactone compound is produced by batchwise chromatog. or pseudo-moving bed method both using a column filled with a packing material for optical resolution comprising a polysaccharide derivative The pseudo-moving bed method comprises jointing endlessly a number of columns to form a circulating flow path wherein a fluid is forcibly circulated in one direction, providing alternately along the direction of flow of the circulated fluid inlets for feeding the fluid into the column and outlets for drawing the fluid out of the column, moving intermittently the positions of the inlets and the outlets in the direction of flow of the circulated fluid, feeding a solution containing a racemate of a mevalonolactone compound and an eluent into a circulating path through the inlets, and drawing out simultaneously a solution enriched with nonadsorbates and a solution enriched with adsorbates through the outlets.

IT **172336-33-3**
RL: ANT (Analyte); ANST (Analytical study)
(process for producing optically active mevalonolactone compound)
RN 172336-33-3 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry unknown.

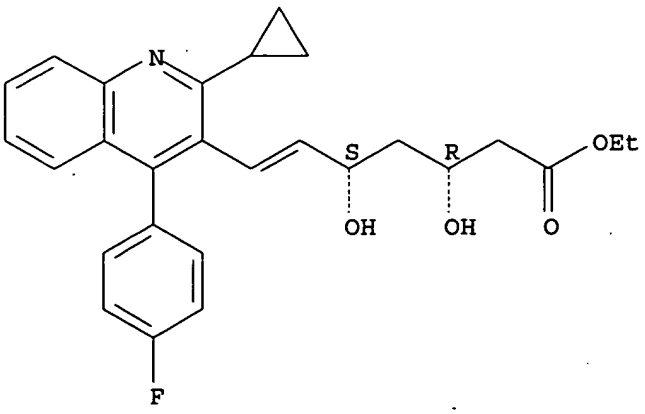


IT **121660-87-5P 172336-32-2P**
RL: **PUR (Purification or recovery); PREP (Preparation)**
(process for producing optically active mevalonolactone compound)
RN 121660-87-5 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester (9CI) (CA INDEX NAME)



RN 172336-32-2 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry unknown.



L67 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:750499 HCAPLUS
DN 123:168993
TI Optically active β-aminoalkoxyborane complex as asymmetric reducing agent
IN Kashihara, Hiroshi; Suzuki, Mikio; Ohara, Yoshio
PA Nissan Chemical Industries Ltd., Japan
SO PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	WO 9417079	A1	19940804		WO 1994-JP56	19940117	<--
	W: AU, CA, CN, CZ, FI, HU, KR, NO, NZ, RO, RU, UA, US						
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
	JP 06329679	A2	19941129		JP 1993-332498	19931227	<--
	TW 383309	B	20000301		TW 1994-83100279	19940114	<--
	AU 9458431	A1	19940815		AU 1994-58431	19940117	<--
	AU 678427	B2	19970529				
	EP 680484	A1	19951108		EP 1994-904332	19940117	<--
	EP 680484	B1	19980819				
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE						
	CN 1116850	A	19960214		CN 1994-190966	19940117	<--
	CN 1047173	B	19991208				
	HU 72018	A2	19960328		HU 1995-2184	19940117	<--
	HU 217182	B	19991228				
	AT 169921	E	19980915		AT 1994-904332	19940117	<--
	RU 2126412	C1	19990220		RU 1995-115845	19940117	<--
	ZA 9400383	A	19940907		ZA 1994-383	19940119	<--
	IL 108387	A1	20000629		IL 1994-108387	19940120	<--
	NO 9502870	A	19950919		NO 1995-2870	19950719	<--
	US 5663348	A	19970902		US 1995-481505	19950719	<--
	US 5767277	A	19980616		US 1997-779621	19970107	<--
	US 5739347	A	19980414		US 1997-848173	19970429	<--
	US 5786485	A	19980728		US 1997-848172	19970429	<--
	US 5808098	A	19980915		US 1997-848169	19970429	<--
	US 5852221	A	19981222		US 1997-848174	19970429	<--
	NO 9805016	A	19950919		NO 1998-5016	19981028	<--
	CN 1234392	A	19991110		CN 1999-105088	19990409	<--
PRAI	JP 1993-7827	A	19930120	<--			
	JP 1993-66825	A	19930325	<--			
	WO 1994-JP56	W	19940117	<--			
	US 1995-481505	A3	19950719	<--			

OS MARPAT 123:168993
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

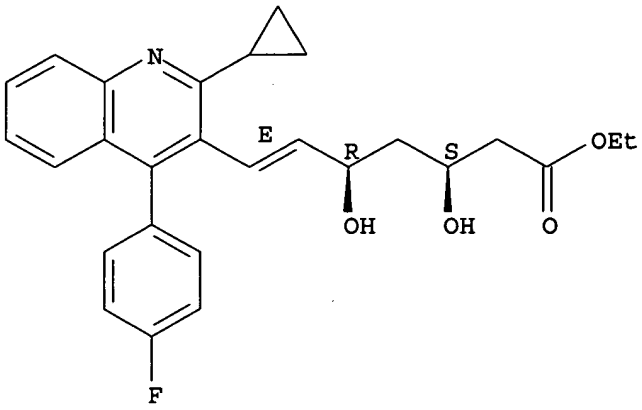
AB Optically active β-aminoalkoxyborane complexes are disclosed, specifically I [R1 = C1-C8 alkyl, C3-C7 cycloalkyl, C7-C11 aralkyl or C6-C10 aryl; R2 = H, C1-C8 alkyl, C3-C7 cycloalkyl or C7-C11 aralkyl; or R1R2 = (CH2)n wherein n = 3 or 4; Ar = naphthyl, anthryl or phenanthryl, which may be substituted by 1-3 substituents selected from halo, nitro, C1-C6 alkyl, C3-C7 cycloalkyl, C2-C6 alkenyl or alkynyl, C7-C11 aralkyl, C6-C10 aryl, C1-C6 alkoxy, and styrene polymer substituents]. The complexes are useful for reducing carbonyl compds. to optically active alcs., and especially for reducing 1,3-dicarbonyl compds. to optically active

1,3-syn-diols. For example, reduction of proline Et ester with LiAlH4 to give (S)-prolinol, cyclocondensation of this with β-naphthaldehyde to give an oxazolidine derivative (quant.), reduction of this with NaBH4 to give an amino alc. (quant.), and reaction of the latter with BH3.THF (quant.), gave the (S)-isomeric complex II. Reduction of diketo ester III using II and Et2BOMe in THF at 20° gave the (3S,5R)-syn-diol IV in 53% yield and 100% enantiomeric excess (ee). In contrast, several similar known borane complexes gave 28-78% yield but only 6-23% ee.

IT **167073-18-9P**, (3S,5R,E)-Ethyl 7-[2-cyclopropyl-4-(p-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate
167073-19-0P, (3R,5S,E)-Ethyl 7-[2-cyclopropyl-4-(p-fluorophenyl)quinolin-3-yl]-3,5-dihydroxy-6-heptenoate
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(reduction product; preparation of optically active β-aminoalkoxyborane complexes for asym. reduction of (di)carbonyl compds.)

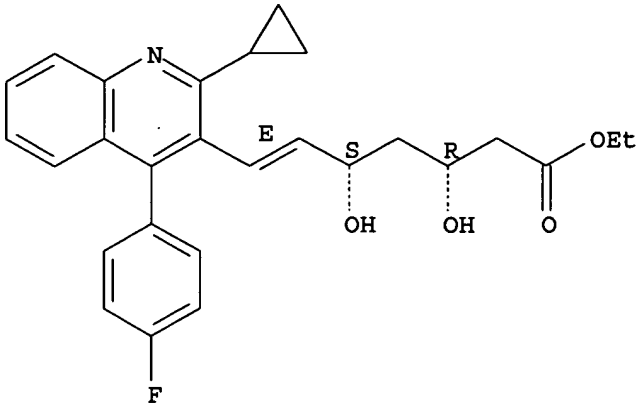
RN 167073-18-9 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3S,5R,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



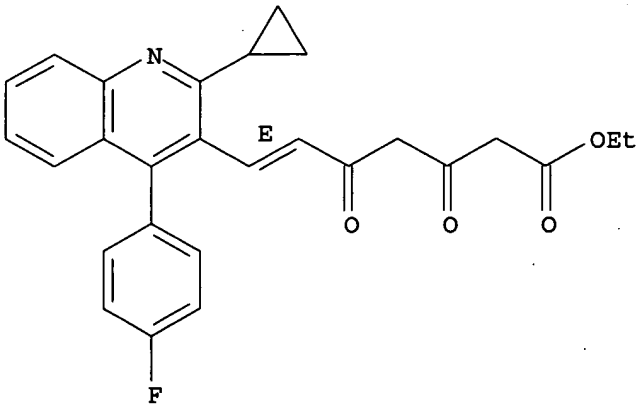
RN 167073-19-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

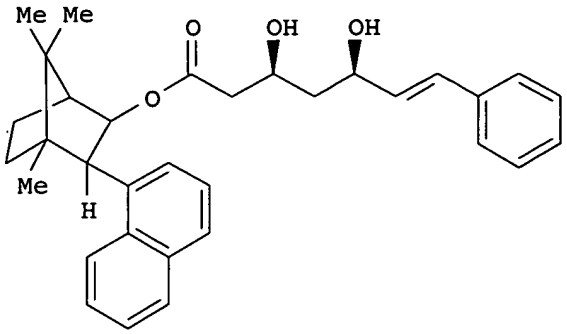


IT **166803-31-2P**, (E)-Ethyl 7-[2-cyclopropyl-4-(p-fluorophenyl)quinolin-3-yl]-3,5-dioxo-6-heptenoate
RL: **IMF (Industrial manufacture)**; RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(reduction substrate; preparation of optically active β-aminoalkoxyborane complexes for asym. reduction of (di)carbonyl compds.)
RN 166803-31-2 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

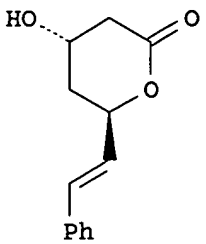
Double bond geometry as shown.



L67 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:330180 HCAPLUS
DN 123:285697
TI Stereoselective reduction of β,δ-diketo esters. A novel strategy for the synthesis of artificial HMG-CoA reductase inhibitors
AU Hiyama, Tamejiro; Reddy, Guntoori Bhaskar; Minami, Tatsuya; Hanamoto, Takeshi
CS Sagami Chem. Research Center, Kanagawa, 229, Japan
SO Bulletin of the Chemical Society of Japan (**1995**), 68(1), 350-63
CODEN: BCSJA8; ISSN: 0009-2673
PB Nippon Kagakkai
DT Journal
LA English
GI



I



II

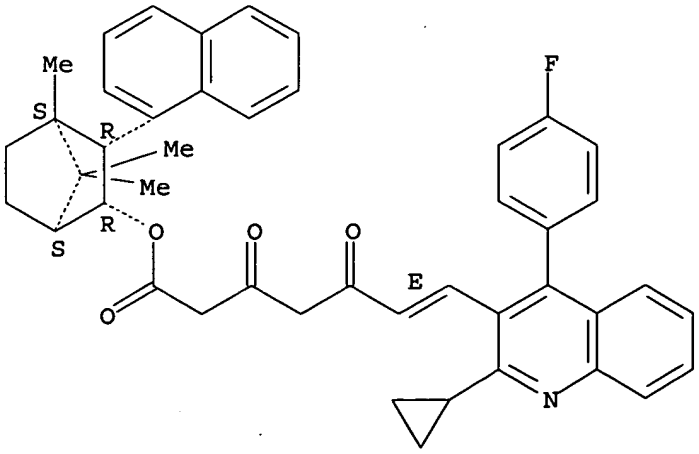
AB Condensation of N-methoxy-N-Me amides with acetoacetate dianions gave β,δ-diketo esters, which were selectively reduced with Et2BOMe-NaBH4 in THF/MeOH to give syn-β,δ-dihydroxy esters in one step. Similarly, the β,δ-diketo esters of the Taber's chiral alc. or its enantiomer resp. were reduced to give syn-β,δ-dihydroxy esters of moderate enantiomeric excess. Higher diastereoselective and enantioselectivity were achieved by reduction of the β,δ-diketo esters of Taber's chiral alc. or its enantiomer successively with diisobutylalane and with Et2BOMe-NaBH4. The resulting syn-diol esters were hydrolyzed and lactonized to give various types of β-hydroxy-δ-lactones commonly found in artificial HMG-CoA reductase inhibitors; pharmacol. test data were not shown. The precursor I was converted to the example compound [4S-[4α,6β(E)]]-tetrahydro-4-hydroxy-6-(2-phenylethenyl)-2H-pyran-2-one (II).

IT **141750-57-4P 141750-58-5P 141750-61-0P 155899-28-8P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation of β-hydroxy-δ-lactones as HMG-CoA reductase inhibitors)

RN 141750-57-4 HCAPLUS

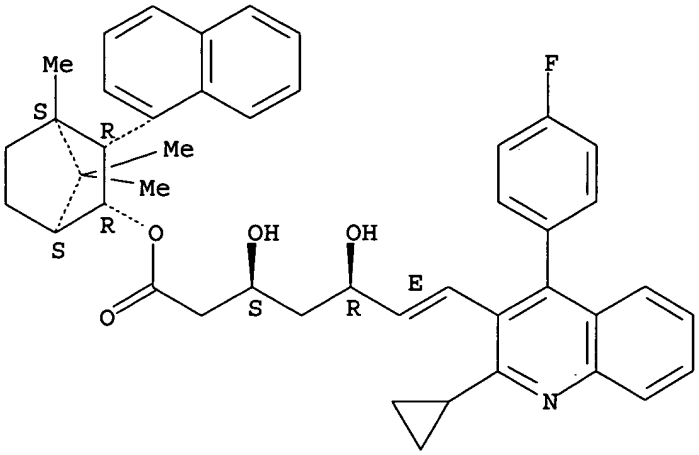
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(E),3α,4α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



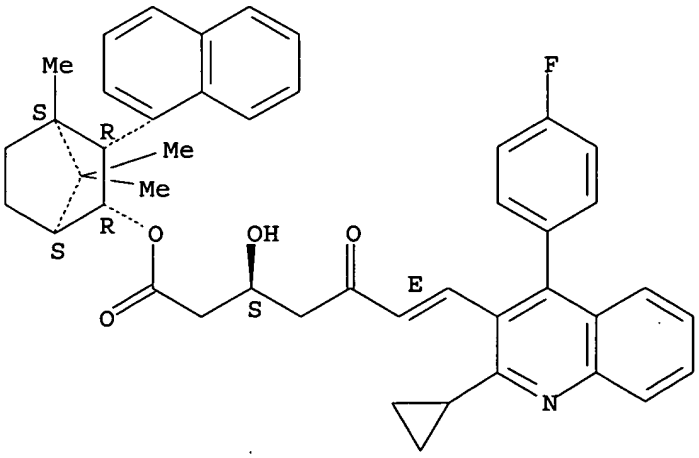
RN 141750-58-5 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(3R*,5S*,6E),3α,4α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



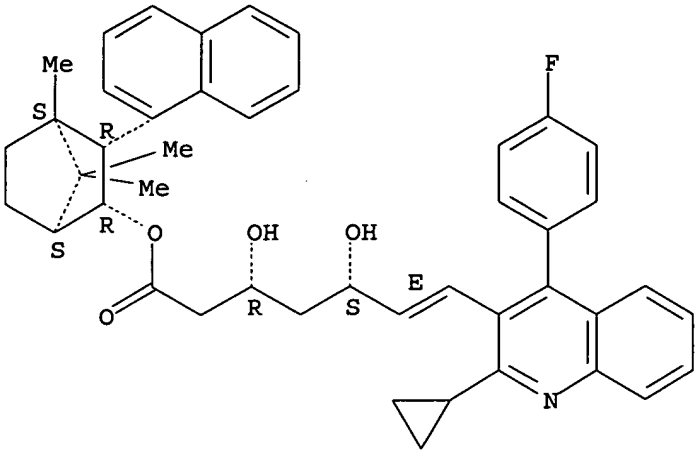
RN 141750-61-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(3R*,6E),3α,4α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 155899-28-8 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(3S*,5R*,6E),3α,4α]]- (9CI) (CA INDEX NAME)

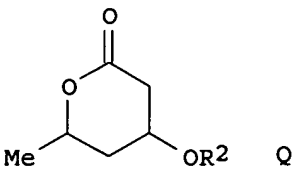
Absolute stereochemistry.
Double bond geometry as shown.



L67 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:304888 HCAPLUS
DN 122:105264
TI preparation of 6-heptynoic and heptenoic acid compounds as intermediates for HMG-CoA reductase inhibitors
IN Hiyama, Tamejiro; Minami, Tatsuya; Takahashi, Kyoko; Miyachi, Nobuhide; Ohara, Yoshio
PA Nissan Chemical Industries Ltd., Japan; Sagami Chemical Research Center
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9406746	A1	19940331	WO 1993-JP1349	19930921 <--
	W: AU, CA, CZ, FI, HU, KR, NO, NZ, RO, RU, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ZA 9306732	A	19940411	ZA 1993-6732	19930913 <--
	JP 06316584	A2	19941115	JP 1993-233018	19930920 <--
	AU 9349845	A1	19940412	AU 1993-49845	19930921 <--
	CN 1088204	A	19940622	CN 1993-117822	19930921 <--
PRAI	JP 1992-251413	A	19920921 <--		
	JP 1993-9489	A	19930122 <--		
	JP 1993-47878	A	19930309 <--		
	WO 1993-JP1349	W	19930921 <--		

OS CASREACT 122:105264; MARPAT 122:105264
GI



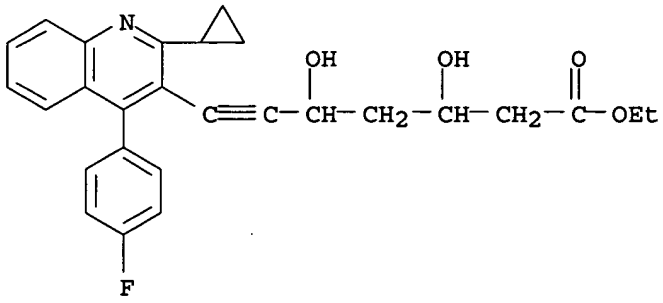
Q

AB Title compds. R6-C.tplbond.C-Z [I; Z = A-CH2-B-CH2-CO-OR1, Q; A = CO, CHOR1; R1 = H, protecting group; B = CO, CHOR2; R2 = H, protecting group; or R1R2 = part of a ring; R3 = H, C1-8 alkyl, aralkyl, aryl, silyl, etc.; R6 = H, protecting group], useful as intermediates for HMG-CoA reductase inhibitors, are prepared The use of the invention compds. and process

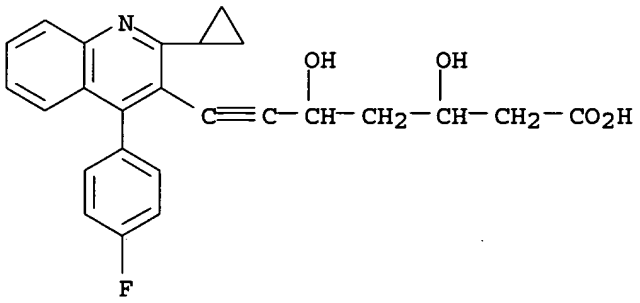
enables an efficient production of a 7-substituted-3,5-dihydroxy carboxylic acid compound useful as an HMG-CoA reductase inhibitor. E.g., I [R6 = trimethylsilyl (TMS), Z = CH(OH)-CH2-CH(OH)-CH2-CO-OEt] was prepared via condensation of TMS-C.tplbond.C-CHO (preparation given) with Et acetoacetate.

IT **156782-70-6P 160375-26-8P 160375-27-9P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of, as intermediate for HMG-CoA reductase inhibitors)

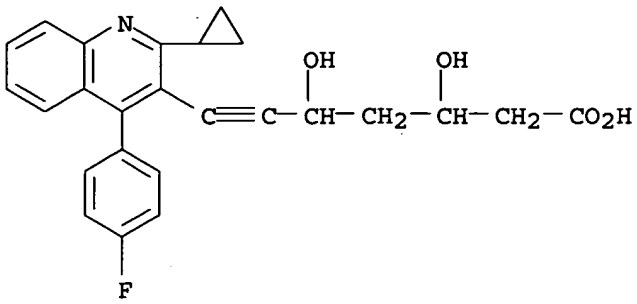
RN 156782-70-6 HCAPLUS
CN 6-Heptynoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



RN 160375-26-8 HCAPLUS
CN 6-Heptynoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)



RN 160375-27-9 HCAPLUS
CN 6-Heptynoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1) (9CI) (CA INDEX NAME)



●1/2 Ca

L67 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:508553 HCAPLUS
DN 121:108553
TI Preparation of 7-(4-phenyl-3-quinolinyl)-3,5-dihydroxyhept-6-ynoic acid derivatives as 3-hydroxy-3-methylglutaric acid coenzyme A (HMG-CoA) reductase inhibitors
IN Obara, Yoshio; Myaji, Nobuhide; Kitahara, Maki
PA Nissan Chemical Ind Ltd, Japan
SO Jpn. Kokai Tokkyo Koho, 39 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
PI	JP 06116239	A2	19940426		JP 1992-266264	19921005 <--
PRAI	JP 1992-266264		19921005	<--		

OS MARPAT 121:108553
GI

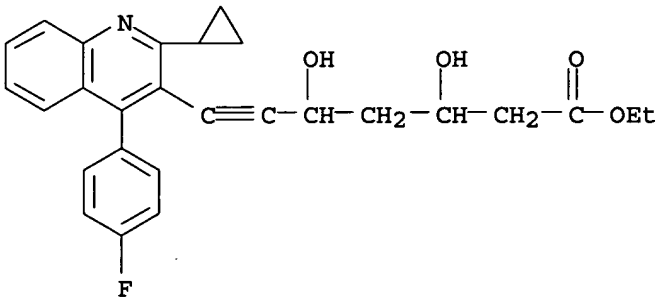
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; X = 5- to 6-membered heteroaryl or (un)substituted Ph ring; R1, R2 = H, C1-8 alkyl, C3-7 cycloalkyl, C1-3 alkoxy, BuO, iso-, sec-, or tert-BuO, R20R21N (wherein R20, R21 = H, C1-3 alkyl), CF3, CF3O, CF2H, F, Cl, Br, Ph, PhO, PhCH2O, OH, Me3SiO, Me3CPh2SiO, HOCH2, O(CH2)lOR22 (wherein R22 = H, C1-3 alkyl; l = 1,2,3); adjacent R1 and R2 form CH:CHCH:CH or OCH2O; R3 = H, C1-8 alkyl, C2-6 alkenyl, C3-7 cycloalkyl, C5-7 cycloalkenyl, (un)substituted Ph, C1-3 alkyl substituted by Ph and 0-2 C1-3 alkyl; Z = Z1CH2WCH2CO2R12, Q, Q1, Q2; Z1 = CO, C(OR13)2, CHOH; W = CO, C(OR13)2, CR11OH; R11 = H, C1-3 alkyl; R12 = H, alkyl of chemical or physiol. hydrolyzable alkyl ester, NHR23R24R25 (wherein R23, R24, R25 = H, C1-4 alkyl), Na, K, 1/2Ca; R13 = primary or secondary C1-6 alkyl or 2R13 = CH2CH2 or (CH2)3; R15, R16 = H, C1-3 alkyl or R15R16 = CH2CH2 or (CH2)3], useful for the treatment of hypercholesteremia, hyperlipoproteinemia, and atheromatous arteriosclerosis, are prepared Thus, 3-cyclopropyl-4-(4'-fluorophenyl)-3-iodoquinoline 60, CuI 8, Pd(PPh3)2Cl2 13, and 0.8 mL Et2NH were added to 42 mg Et 3,5-O-isopropylidene-3,5-dihydroxy-6-heptynoate followed by stirring at room temperature for 4 h to give 36% phenylquinoline derivative (II; RR = CMe2; M = Et) which was treated with p-MeC6H4SO3H in aqueous THF to give II (R = H; M = Et) (III). The latter

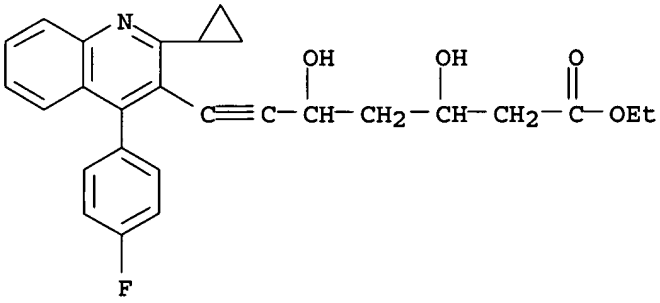
ester was saponified by aqueous 1 N NaOH and EtOH followed by acidification with
aqueous 1 N HCl and conversion of the resulting free carboxylic acid to Ca salt to give II.1/2Ca (R = M = H) (IV). III and IV at 100 nM in vitro inhibited 43.8 and 54.6%, resp., the cholesterol synthesis from AcOH in rat liver microsome prepn, in which HMG-CoA reductase is the rate determining enzyme. Tablet, capsule, ointment, suppository, injection, and granule formulations containing III were described.

IT **156782-70-6P 156782-72-8P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of, as HMG-CoA reductase inhibitor)

RN 156782-70-6 HCAPLUS
CN 6-Heptynoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



RN 156782-72-8 HCAPLUS
CN 6-Heptynoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, calcium salt (2:1) (9CI) (CA INDEX NAME)



●1/2 Ca

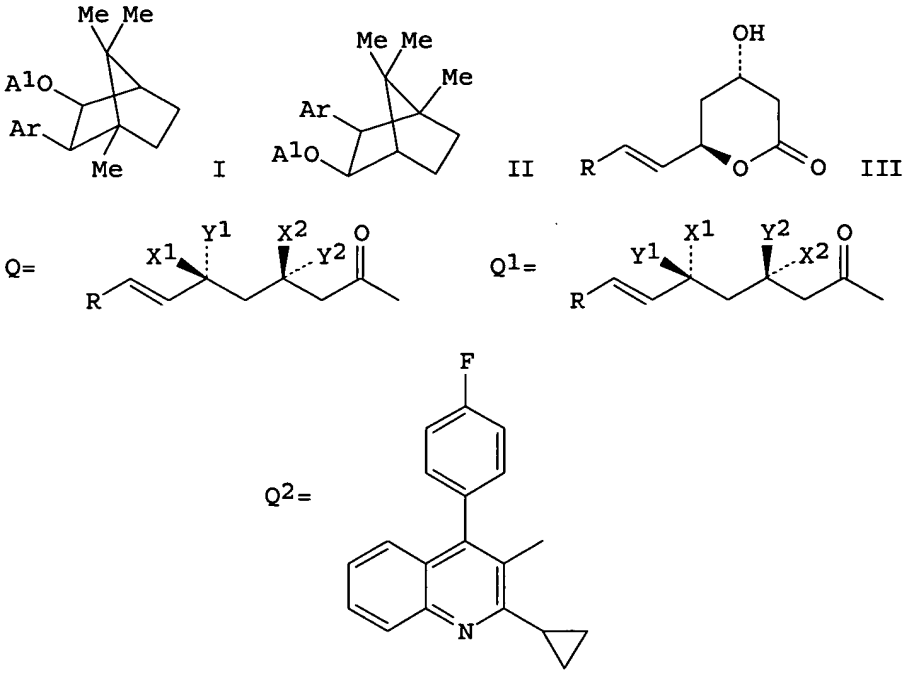
L67 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:435341 HCAPLUS
DN 121:35341
TI Preparation of optically active β,δ-diketo acid derivatives
IN Hyama, Tamejiro; Minami, Tatsuya; Guntoori, Basukaaru Redei; Sakota, Ryozo; Arai, Kazutaka; Obara, Yoshio; Suzuki, Mikio
PA Sagami Chem Res, Japan; Nissan Chemical Ind Ltd
SO Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DT Patent
LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06025092	A2	19940201	JP 1991-291586	19911107 <--
PRAI	JP 1991-291586		19911107 <--		

OS CASREACT 121:35341; MARPAT 121:35341

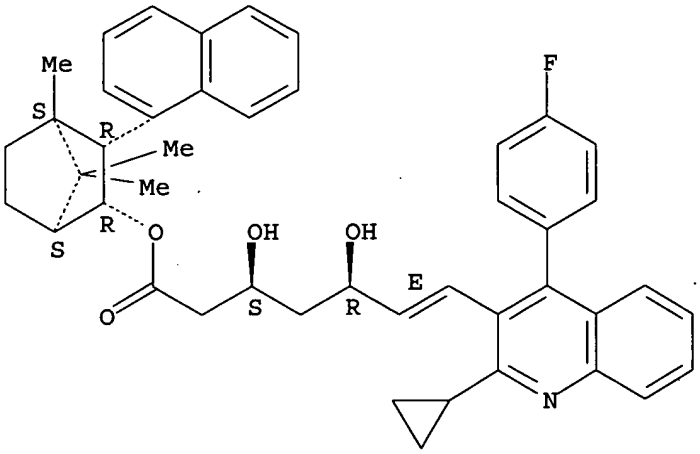
GI



AB 2-Exo-(hetero)arylheptenoyloxy-3-exo-aryl-4,7,7-trimethylbicyclo[2.2.1]heptane derivs. [I; A1 = (un)substituted (hetero)aryl or vinyl; Ar = condensed aryl; X1, Y1 = H, OH or X1Y1 = O; X2, Y2 = H, OH or X2Y2 = O] and enantiomers thereof are prepared by treatment of acetoacetate derivs. I (A1 = MeCOCH2CO) with a base to generate a dianion followed by condensation with N-alkoxyamides trans-RCH:CHCONR1OR2 (Ar = same as above; R1, R2 = C1-4 linear or branched alkyl) and stereoselective reduction of the resulting β,δ-diketo acid derivs. I (A1 = trans-RCH:CHCOCH2COCH2CO). These derivs. I are useful as intermediates for 7-(R-substituted)-(E,3R,5S)-3,5-dihydroxy-6-heptenoic acid 1,5-lactones, hypocholesteremics, having hydroxymethylglutaryl-CoA (HMG-CoA) reductase-inhibitory activity. Thus, acetoacetate ester II (Ar = 2-naphthyl, A1 = MeCOCH2CO) was treated with NaH in THF at 0° followed by addition of BuLi/hexane at 0° and cooling to -78° and a solution of a N-methoxy-N-methylamide trans-RCH:CHCONMeOMe (R = Q2) (preparation given) in THF was added to give, after stirring at -78° to 0° for 3 h, 48% quinolyldioxoheptenoic acid derivative I (A1 = trans-RCH:CHCOCH2COCH2CO, R = Q2, Ar = 2-naphthyl). The latter compound was reduced by NaBH4 in the presence of Et2BOMe in THF/MeOH at -78° to room temperature to give quinolyldihydroxyheptenoic acid ester 90% (A1 = Q1, R = Q2, X1 = X2 = OH, Y1 = Y2 = H, Ar = 2-naphthyl) which was saponified with aqueous NaOH in MeOH and lactonized by refluxing in toluene to give lactone III (R = Q2) of 58% e.e. as a 77:23 mixture of trans/cis isomers.

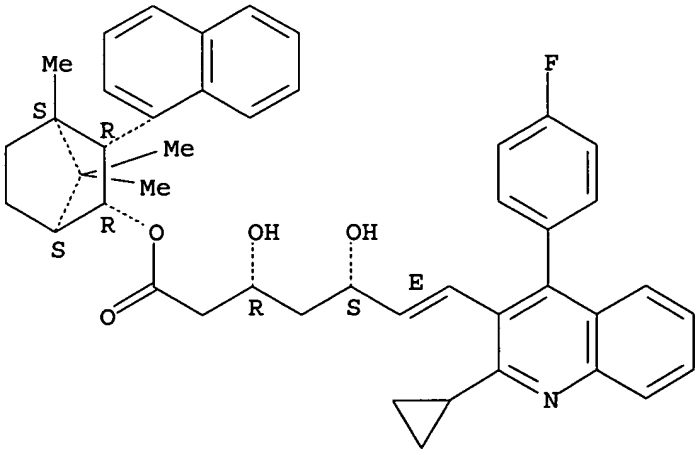
IT **141750-58-5P 155899-28-8P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and saponification-lactonization of)
RN 141750-58-5 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(3R*,5S*,6E),3α,4α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 155899-28-8 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(3S*,5R*,6E),3α,4α]]- (9CI) (CA INDEX NAME)

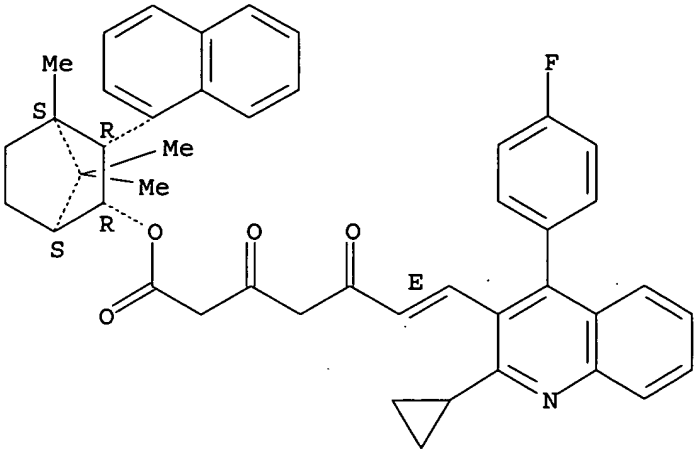
Absolute stereochemistry.
Double bond geometry as shown.



IT **141750-57-4P 141750-61-0P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and stereoselective reduction of)
RN 141750-57-4 HCAPLUS

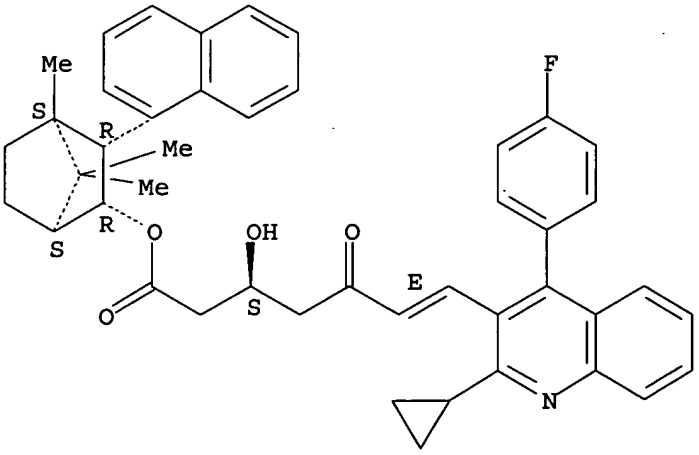
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(E),3α,4α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 141750-61-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(3R*,6E),3α,4α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

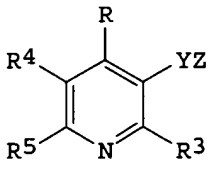


L67 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:517112 HCAPLUS
DN 119:117112
TI Preparation of (heterocyclylvinyl)mevalonic lactone analogs as antiatherosclerotics
IN Saito, Yasushi; Kitahara, Masaki; Sakashita, Mitsuaki; Toyoda, Kyomi; Shibazaki, Toshie
PA Nissan Chemical Industries, Ltd., Japan; Kowa Co., Ltd.
SO Eur. Pat. Appl., 64 pp.
CODEN: EPXXDW

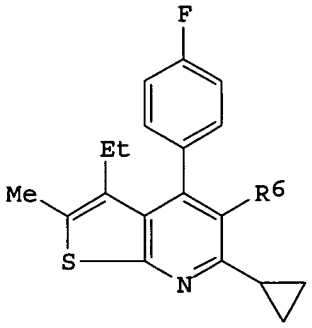
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	EP 535548	A1	19930407	EP 1992-116417	19920924	<--
	EP 535548	B1	20011121			
	R: AT, BE, CH, DE, DK, FR, GB, IE, IT, LI, LU, NL, SE					
	JP 06329540	A2	19941129	JP 1991-257870	19911004	<--
	JP 3130342	B2	20010131			
	AT 209035	E	20011215	AT 1992-116417	19920924	<--
	AU 9226012	A1	19930408	AU 1992-26012	19920928	<--
	AU 652669	B2	19940901			
	NZ 244555	A	20000623	NZ 1992-244555	19920930	<--
	US 6162798	A	20001219	US 1992-953716	19920930	<--
	NO 9203858	A	19930405	NO 1992-3858	19921002	<--
	CA 2079706	AA	19930415	CA 1992-2079706	19921002	<--
	HU 62794	A2	19930628	HU 1992-3138	19921002	<--
	HU 214624	B	19980428			
	CZ 281786	B6	19970115	CZ 1992-3027	19921002	<--
	RU 2114620	C1	19980710	RU 1992-5052949	19921002	<--
	SK 279277	B6	19980909	SK 1992-3027	19921002	<--
PRAI	JP 1991-257870	A	19911004	<--		

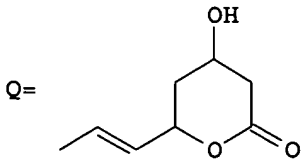
OS MARPAT 119:117112
GI



I

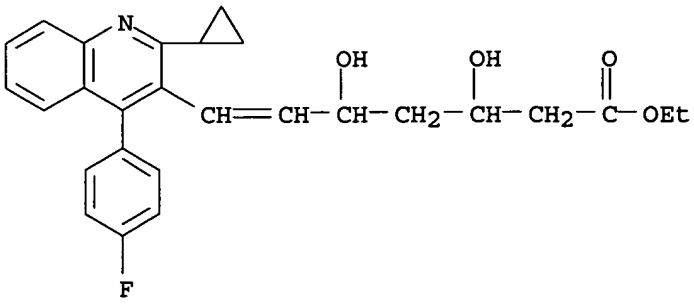


II



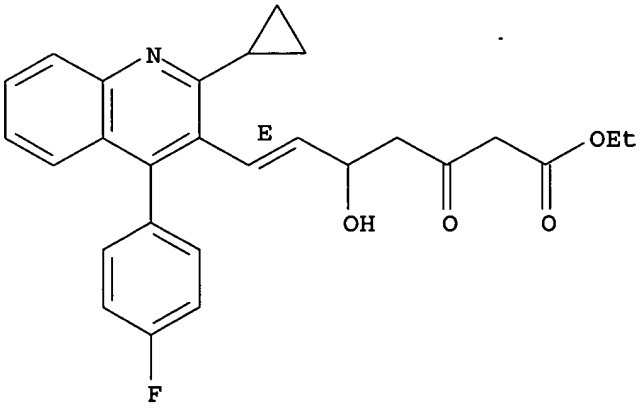
AB Title compds. [I; R = substituted-Ph; R3 = H, (cyclo)alkyl, (cyclo)alkenyl, (substituted)Ph, etc.; R4R5 = atoms to complete a fused benzene or 5- or 6-membered heteroaryl ring; Y = CH2, CH2CH2, CH:CH, etc.; Z = 4-hydroxy-2-oxo- or 2,4-dioxo-6-tetrahydropyranyl, QCH2WCH2CO2R12, etc.; Q = CO, CH(OH), etc.; R12 = H, ammonium, physiol. labile ester residue, etc.; W = CO, CH(OH), etc.], inhibitors of atherosclerotic intimal thickening, were prepared Thus, thienopyridinecarboxyaldehyde II (R6 = CHO) was condensed with Bu3SnC(OEt):CH2 and the product hydrolyzed to give II [R6 = (E)-CH:CHCHO] which was condensed with MeCOCH2CO2Et to give, in 3 addnl. steps, II (R6 = oxopyranylvinyl group Q). The latter gave 100% inhibition of smooth muscle cell proliferation at 10-6 M (intimal) and 10-5 M (medial) in vitro.

IT **121661-13-0P 148901-69-3P**
RL: RCT (Reactant); **SPN (Synthetic preparation); PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and reaction of, in preparation of antiatherosclerotic)
RN 121661-13-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)

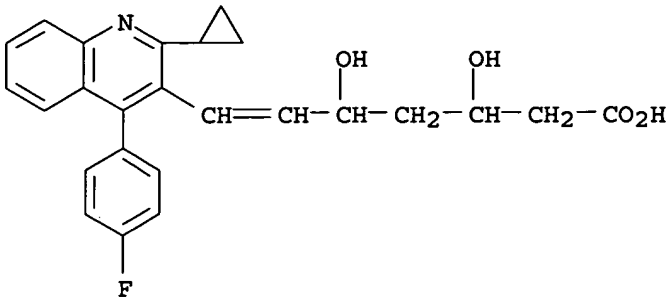


RN 148901-69-3 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester, (6E)- (9CI) (CA INDEX NAME)

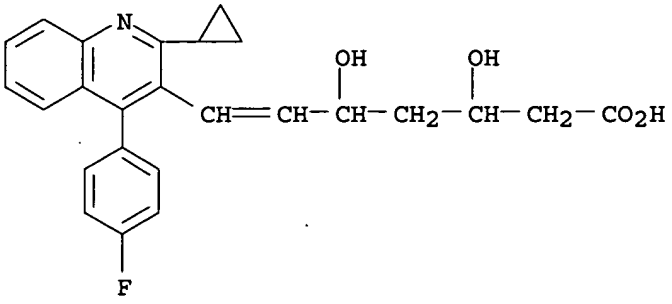
Double bond geometry as shown.

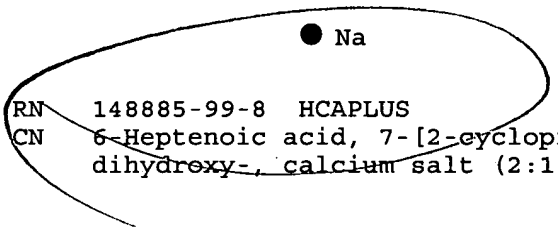


IT **121659-03-8P 121659-04-9P 148885-99-8P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of, as antiatherosclerotic)
RN 121659-03-8 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)

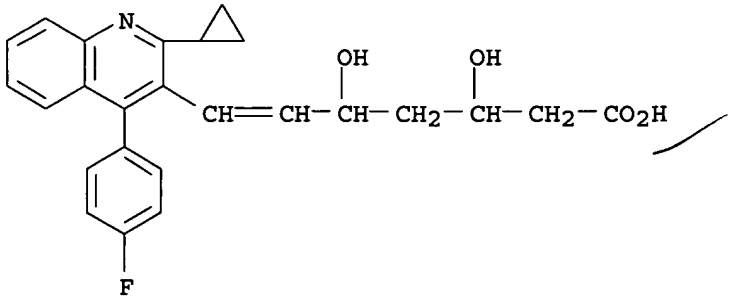


RN 121659-04-9 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, monosodium salt (9CI) (CA INDEX NAME)





RN 148885-99-8 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1) (9CI) (CA INDEX NAME)

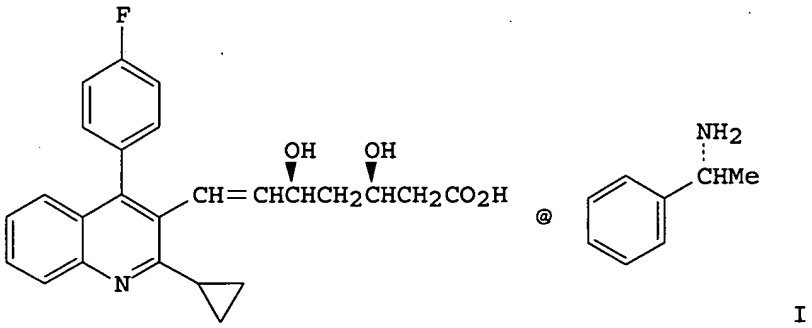


L67 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:233897 HCAPLUS
DN 118:233897
TI Preparation of diastereomer salt of optically active quinolinemevalonic

acid
IN Ohara, Yoshio; Suzuki, Mikio; Yanagawa, Yoshinobu; Iwasaki, Hiroshi; Miyachi, Nobuhide
PA Nissan Chemical Industries, Ltd., Japan
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	EP 520406	A1	19921230		EP 1992-110636	19920624	<--
	EP 520406	B1	19980902				
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE						
	JP 05148237	A2	19930615		JP 1992-127277	19920520	<--
	JP 3528186	B2	20040517				
	CA 2072162	AA	19921225		CA 1992-2072162	19920623	<--
	CA 2072162	C	20021119				
	US 5284953	A	19940208		US 1992-902863	19920623	<--
	EP 742209	A2	19961113		EP 1996-107815	19920624	<--
	EP 742209	A3	19970514				
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, PT, SE						
	AT 170513	E	19980915		AT 1992-110636	19920624	<--
	ES 2120973	T3	19981116		ES 1992-110636	19920624	<--
	US 5473075	A	19951205		US 1993-123117	19930920	<--
	US 5514804	A	19960507		US 1995-450383	19950525	<--
PRAI	JP 1991-151810	A	19910624	<--			
	JP 1992-127277	A	19920520	<--			
	US 1992-902863	A3	19920623	<--			
	EP 1992-110636	A3	19920624	<--			
	US 1993-123117	A3	19930920	<--			

GI



I

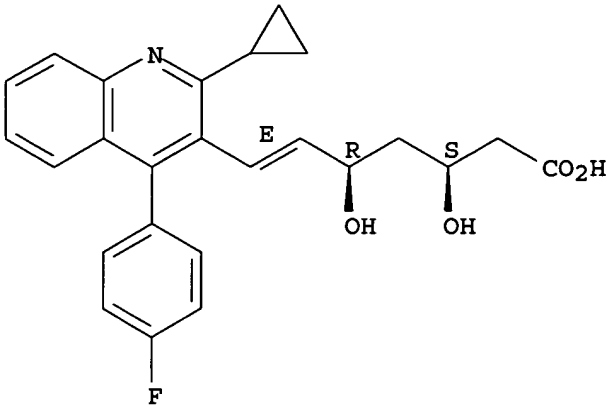
AB A diastereomer salt of the title compound (I) which is an intermediate for preparation of optically active quinolinemevalonic acid derivs. with known. biol. activity is prepared by resolution of its racemic parent. Et (±)-(E)-3,5-dihydroxy-7-[4-(4-fluorophenyl)-2-cyclopropyl-3-quinolinyl]-6-heptenoate in EtOH was added to 1N NaOH to give the free acid. To the CH2Cl2 solution of the free acid 1 equiv of D-(+)-PhCH(NH2)Me was added to give the (E)-(3R,5S)-I.

IT **147008-21-7P**
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation and resolution of)

RN 147008-21-7 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-

dihydroxy-, [R*,S*-(E)]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

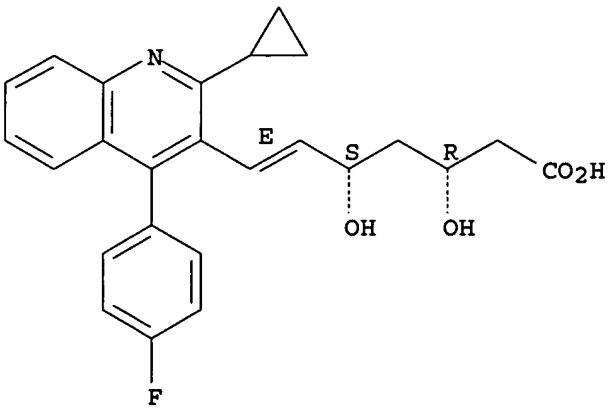


IT **147511-70-4P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and ring closure of)
RN 147511-70-4 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, (3R,5S,6E)-, compd. with (αR)-α-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 147511-69-1
CMF C25 H24 F N O4

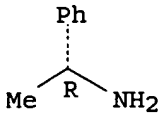
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

CRN 3886-69-9
CMF C8 H11 N

Absolute stereochemistry.

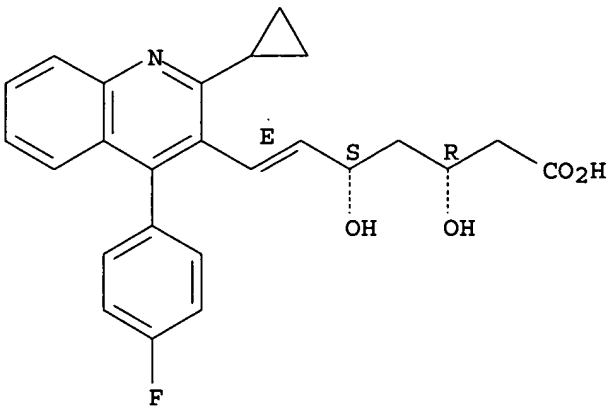


IT **147511-71-5P 147511-72-6P 147526-32-7P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of)
RN 147511-71-5 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, [S-[R*,S*-(E)]]-, compd. with (R)-α,4-dimethylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 147511-69-1
CMF C25 H24 F N O4

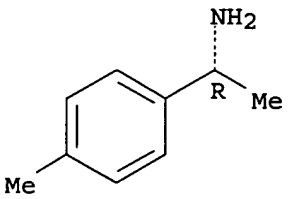
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

CRN 4187-38-6
CMF C9 H13 N

Absolute stereochemistry. Rotation (+).

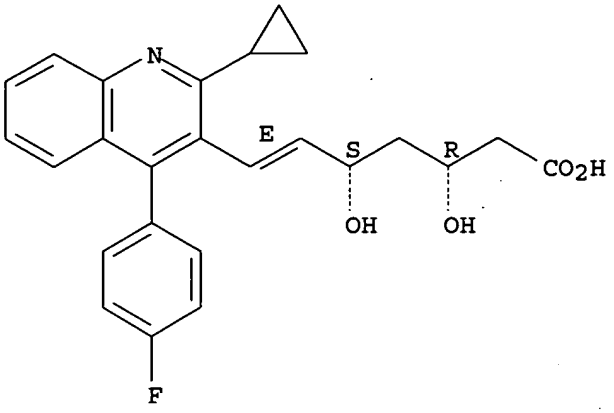


RN 147511-72-6 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, [S-[R*,S*-(E)]]-, compd. with (R)-2-amino-1-butanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 147511-69-1
CMF C25 H24 F N O4

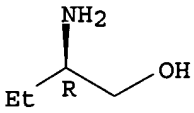
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



CM 2

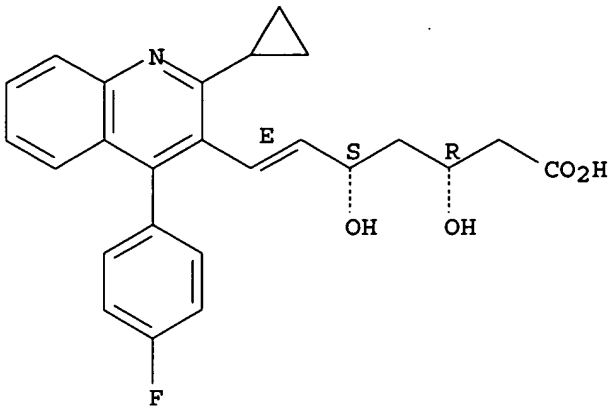
CRN 5856-63-3
CMF C4 H11 N O

Absolute stereochemistry. Rotation (-).



RN 147526-32-7 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, calcium salt (2:1), (3R,5S,6E)- (9CI) (CA INDEX NAME)

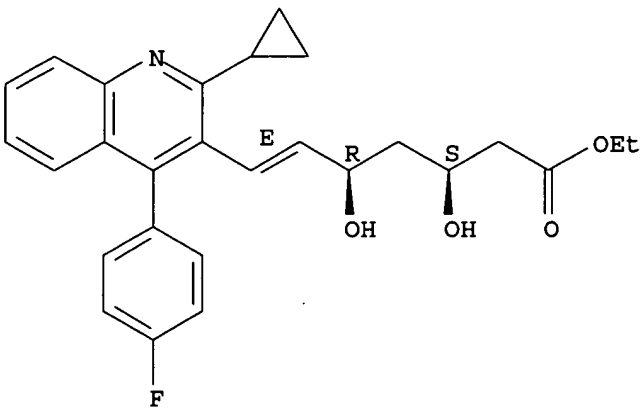
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



●1/2 Ca

IT **147008-20-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(saponification of)
RN 147008-20-6 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester, (3R,5S,6E)-rel- (9CI) (CA INDEX NAME)

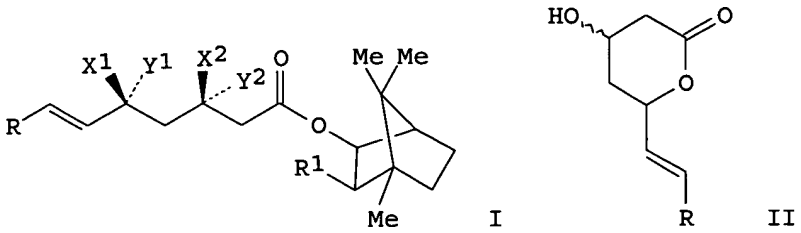
Relative stereochemistry.
Double bond geometry as shown.



L67 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:407804 HCAPLUS
DN 117:7804
TI Optically active esters of 7-substituted 3,5-difunctionalized 6-heptenoic acids
IN Hiyama, Tamejiro; Minami, Tatsuya; Hanamoto, Takeshi; Reddy, Guntoori Bhaskar
PA Sagami Chemical Research Center, Japan
SO Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

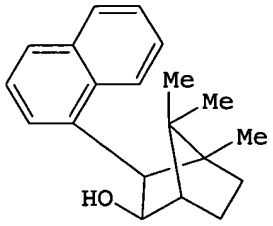
	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	EP 475627	A1	19920318		EP 1991-307837	19910828	<--
	EP 475627	B1	19941019				
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE						
	JP 05004943	A2	19930114		JP 1991-214148	19910801	<--
	US 5276154	A	19940104		US 1991-748076	19910821	<--
	HU 58267	A2	19920228		HU 1991-2818	19910829	<--
	HU 209583	B	19940829				
	CA 2050266	AA	19920301		CA 1991-2050266	19910829	<--
	US 5369109	A	19941129		US 1993-77454	19930617	<--
PRAI	JP 1990-226741		19900830	<--			
	JP 1991-214148		19910801	<--			
	US 1991-748076		19910821	<--			
OS	MARPAT 117:7804						

GI



I

II



III

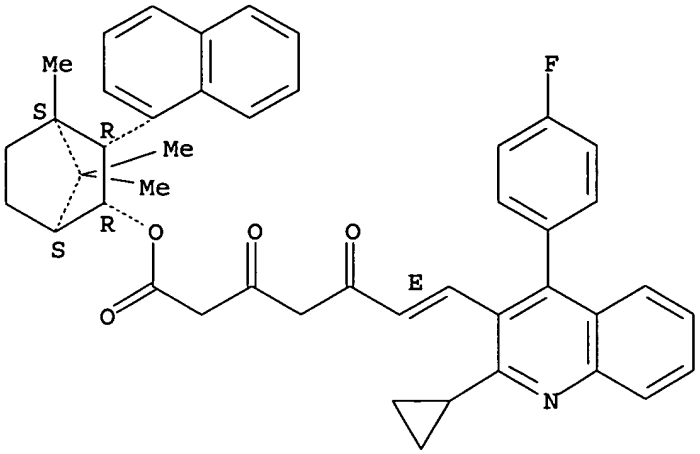
AB Title esters I [R = (un)substituted aromatic, heteroarom., substituted vinyl; R1 = condensed aromatic; X1 = H, Y1 = OH, X1 = OH, Y1 = H, X1Y1 = O; X2 = H, Y2 = OH, X2 = OH, Y2 = H, X2Y2 = O] were prepared as intermediates for the HMG-CoA reductase-inhibiting heptenolides II. Thus, (-)-camphor was converted to the alc. III in 5 steps. III was converted to its acetoacetate and heated with (E)-PhCH:CHCONMeOMe to give I (R = Ph, R1 = 1-naphthyl, X1Y1, X2Y2 = O). The latter compound was reduced by MeOBEt2 to I (R = Ph, R1 = 1-naphthyl, X1, X2 = H, Y1, Y2 = OH) which was hydrolyzed to (3S,5R)-II (R = Ph).

IT **141750-57-4P 141750-61-0P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and stereoselective reduction of)

RN 141750-57-4 HCAPLUS

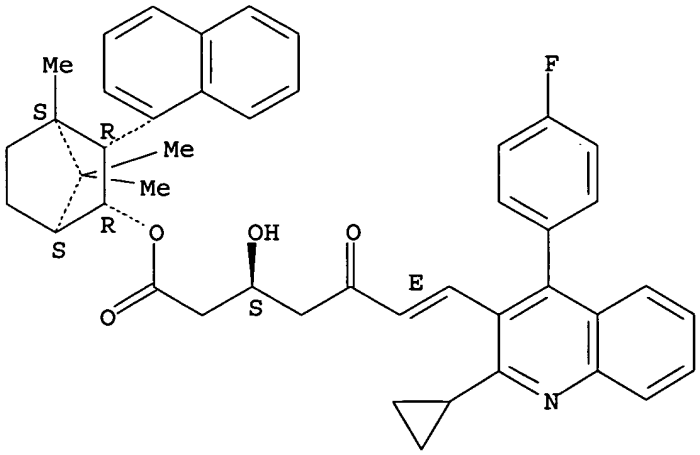
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dioxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(E),3α,4α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



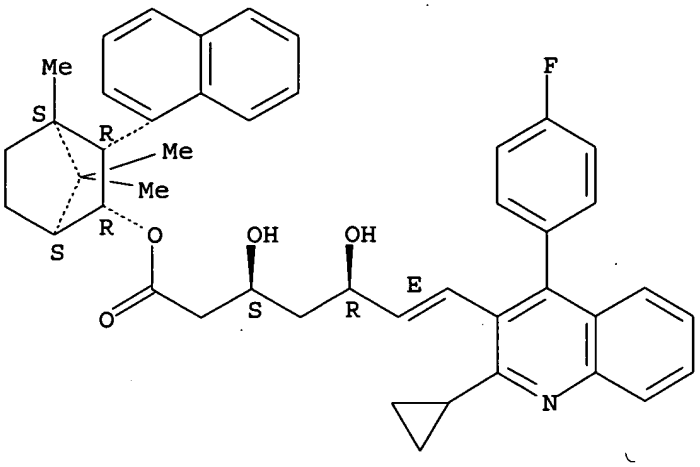
RN 141750-61-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3-hydroxy-5-oxo-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(3R*,6E),3α,4α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

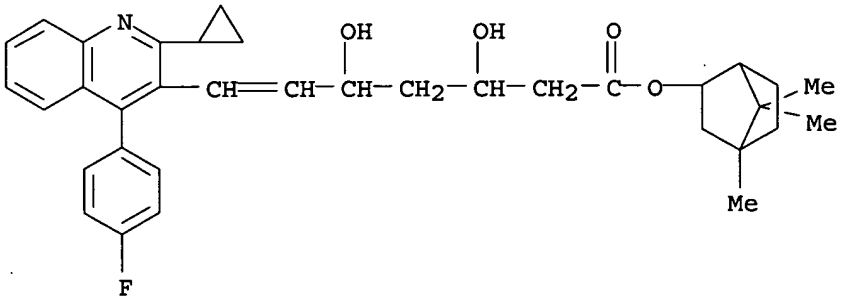


IT **141750-58-5P 141750-62-1P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation, hydrolysis, and lactonization of)
RN 141750-58-5 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 4,7,7-trimethyl-3-(1-naphthalenyl)bicyclo[2.2.1]hept-2-yl ester, [1S-[1α,2α(3R*,5S*,6E),3α,4α]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 141750-62-1 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, 4,7,7-trimethylbicyclo[2.2.1]hept-2-yl ester, [1S-[1α(3S*,5R*,6E),4α]]- (9CI) (CA INDEX NAME)



L67 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:534010 HCAPLUS
DN 111:134010
TI Quinolinylheptenoic acid derivatives as anticholesteremics, their preparation, and formulations containing them
IN Fujikawa, Yoshihiro; Suzuki, Mikio; Iwasaki, Hiroshi; Sakashita, Mitsuaki; Kitahara, Masaki
PA Nissan Chemical Industries, Ltd., Japan
SO Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 304063	A2	19890222	EP 1988-113448	19880818 <--
	EP 304063	A3	19901003		
	EP 304063	B1	19941130		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 01279866	A2	19891110	JP 1988-193606	19880803 <--
	JP 2569746	B2	19970108		
	CA 1336714	A1	19950815	CA 1988-574999	19880817 <--
	ES 2067460	T3	19950401	ES 1988-113448	19880818 <--
	US 5011930	A	19910430	US 1990-483720	19900223 <--

	US 5102888	A	19920407	US 1990-483724	19900223 <--
	US 5185328	A	19930209	US 1990-483829	19900223 <--
	US 5872130	A	19990216	US 1990-631092	19901219 <--
	US 5856336	A	19990105	US 1992-883398	19920515 <--
	US 5854259	A	19981229	US 1992-978884	19921119 <--

PRAI JP 1987-207224 19870820 <--
JP 1988-15585 19880126 <--
JP 1988-193606 19880803 <--
US 1988-233752 19880819 <--
US 1990-631092 19901219 <--
US 1992-883398 19920515 <--

OS MARPAT 111:134010

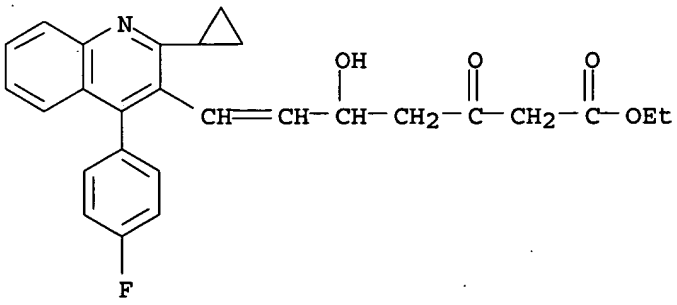
GI For diagram(s), see printed CA Issue.

AB The title compds. I [R1-R4, R6 = H, C1-6 alkyl, C3-6 cycloalkyl, C1-3 alkoxy, etc.; or R1 and R2, R3 and R4 may form CH:CHCH:CH, etc.; Y = CH2, CH2CH2, CH:CH, CH2CH:CH, CH:CHCH2; Z = QCH2WCH2CO2R12, Q1, etc.; Q = C(O), CH(OH), etc.; W = C(O), C(R11)(OH), etc.; R11 = H, C1-6 alkyl; R12 = H, R14; R14 = physiol. hydrolyzable alkyl, M; M = NH4, Na, K, etc.; R5 = H, C1-6 alkyl, C2-3 alkenyl, C3-6 cycloalkyl, etc.], useful as cholesterol biosynthesis inhibitors, were prepared Reduction of Et (E)-7-[4'-(4''-fluorophenyl)-2'-(1'''-methylethyl)quinolin-3'-yl]-5-hydroxy-3-oxohept-6-enoate (preparation given) with NaBH4, followed by saponification in 0.5N NaOH, gave (E)-3,5-dihydroxy-7-[4'-(4''-fluorophenyl)-2'-(1'''-methylethyl)-quinolin-3'-yl]-hept-6-enoic acid Na salt (II). II exhibited an IC50 of 1.0 + 10-8M against cholesterol biosynthesis from acetate in vitro. A capsule formulation containing II 1, lactose 3.5, cellulose 10, Mg stearate 0.5 g is given.

IT **121660-87-5P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and reaction of, in preparation of cholesterol biosynthesis inhibitor)

RN 121660-87-5 HCAPLUS

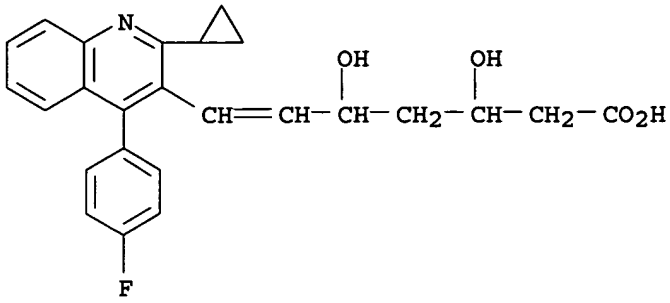
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-5-hydroxy-3-oxo-, ethyl ester (9CI) (CA INDEX NAME)



IT **121659-03-8P 121659-04-9P 121659-23-2P**
121661-13-0P 121678-77-1P
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of, as cholesterol biosynthesis inhibitor)

RN 121659-03-8 HCAPLUS

CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)



RN 121659-04-9 HCAPLUS
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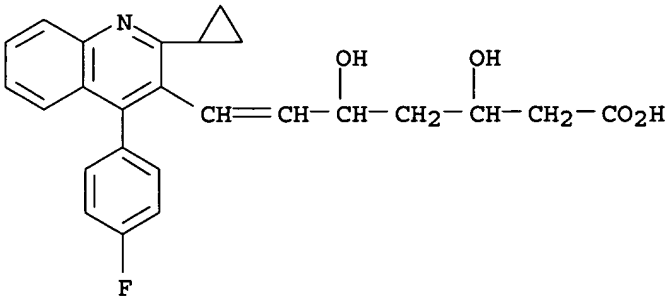
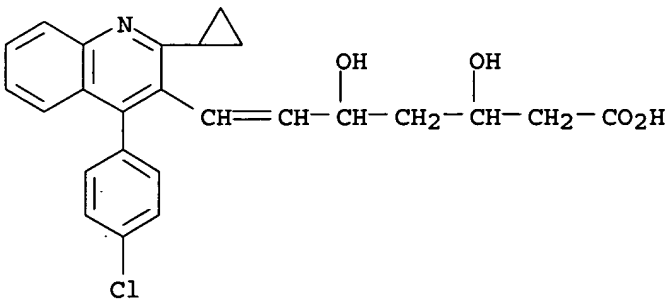
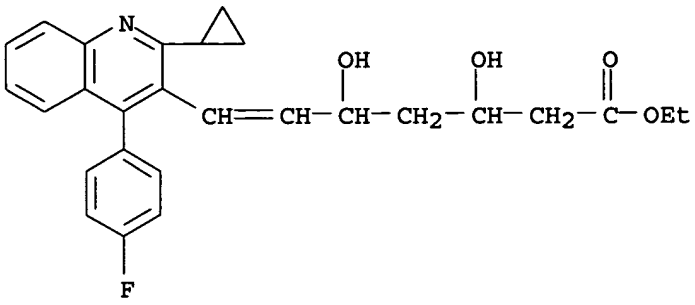


● Na

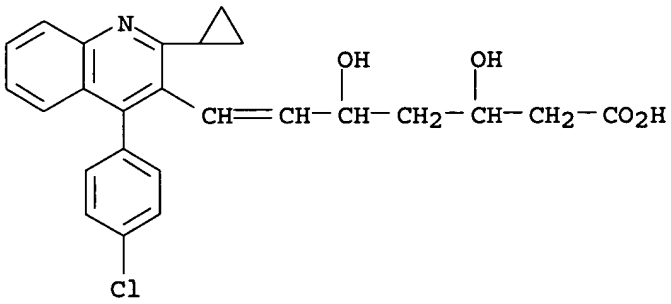
RN 121659-23-2 HCAPLUS
CN 6-Heptenoic acid, 7-[4-(4-chlorophenyl)-2-cyclopropyl-3-quinolinyl]-3,5-dihydroxy- (9CI) (CA INDEX NAME)



RN 121661-13-0 HCAPLUS
CN 6-Heptenoic acid, 7-[2-cyclopropyl-4-(4-fluorophenyl)-3-quinolinyl]-3,5-dihydroxy-, ethyl ester (9CI) (CA INDEX NAME)



RN 121678-77-1 HCAPLUS
CN 6-Heptenoic acid, 7-[4-(4-chlorophenyl)-2-cyclopropyl-3-quinolinyl]-3,5-dihydroxy-, monosodium salt (9CI) (CA INDEX NAME)



● Na

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